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Occupational Exposures and Asthma in Domestic Cleaning Women

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Occupational Exposures and Asthma in Domestic Cleaning Women

Departament de Ciències Experimentals i de la Salut

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An ancient Indian proverb suggests
a universal law: cleaning something
is always involved with dirtying
something else

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Inevitablemente, cuando pienso en el camino recorrido hasta llegar aquí, multitud de personas, lugares, situaciones cruzan mi mente. No ha sido fácil, pero he contado con el apoyo de muchas personas que me han ayudado en el día a día y a las que quiero expresar mi más sincero agradecimiento.

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PREFACE

The present doctoral thesis consists of the following sections: introduction, rationale, objectives, scientific papers (three), general discussion, overall conclusions, recommendations and future research. The results presented here are part of the "Epidemiological Study of the Risk of Asthma in Cleaning Workers" (EPIASLI study), which began in January 2000 supported by the Spanish Ministry of Science and Technology (grant CICYT/FEDER (2FD97-2071)). The main objective of the EPIASLI study was to investigate relationships between occupational exposures and asthma in cleaning workers, with a special emphasis on domestic cleaning workers. I started working in the EPIASLI study in February 2000 and was involved from the beginning in the study design. I also wrote the study protocol, supervised the fieldwork, did the data management with the assistance of colleagues, performed the statistical analyses and wrote the three scientific papers that constitute this doctoral thesis.

ACRONYMS

ARDS: Adult Respiratory Distress Syndrome

BHR: Bronchial HiperResponsiveness

CI: Confidence Interval

COPD: Chronic Obstructive Pulmonary Disease

ECRHS: European Community Respiratory Health Survey

EPIASLI: *Investigación Epidemiológica del Riesgo de Asma en Trabajadores de Limpieza* (Epidemiological Study of the Risk of Asthma in Cleaning Workers)

FEV_1: Forced Expiratory Volume in one second

FVC: Forced Vital Capacity

IgE: Immunoglobulin E

LRS: Lower Respiratory tract Symptoms

OA: Occupational Asthma

Oasys: Occupational asthma system

OR: Odds Ratio

PEF: Peak Expiratory Flow

RADS: Reactive Airways Dysfunction Syndrome

SD: Stardard Deviation

URS: Upper Respiratory tract Symptoms

SUMMARY

Background: Recent epidemiological studies and surveillance programmes have evidenced an increased risk of asthma in cleaning workers. A population-based study suggested that those employed in domestic cleaning had a particularly high risk. The specific occupational exposures related to asthma in cleaning workers remain unclear.

Main objectives: **(1)** Assess the risk of asthma and other respiratory symptoms in domestic and non-domestic cleaning women; **(2)** identify the specific occupational exposures associated with a higher risk of asthma (and chronic bronchitis) in domestic cleaning women; **(3)** elucidate the immunological or irritant mechanisms involved in cleaning-related asthma by considering the cleaning tasks and products implicated; **(4)** assess the short-term changes in respiratory symptoms and peak expiratory flow (PEF) associated with specific cleaning exposures in domestic cleaning women with respiratory disorders.

Methods: **(1)** Between June 2000 and July 2001 we carried out the first phase of the EPIASLI study, consisting of a population-based cross-sectional survey of 4,521 women living in Cornellà de Llobregat (Barcelona, Spain). Participants were classified according to their cleaning work history and their current respiratory symptoms as reporte respiratory symptoms as reporterisks for asthma and other respiratory symptoms (odds ratios (ORs) and 95% confidence intervals (CIs)) were estimated for the different cleaning groups as compared with those who had never worked in cleaning, using multivariate unconditional logistic regression models.

(2) In a second phase, between June 2001 and April 2002 a nested case-control study was carried out among a subsample of current domestic cleaning women, including 40 cases with symptoms of asthma and/or chronic bronchitis and 155 controls without any history of respiratory symptoms. Detailed information about specific occupational exposures was obtained in a face-to-face interview, and participants underwent lung function, methacholine challenge and serum IgE tests. Personal exposure measurements of airborne chlorine and ammonia were performed in a subsample of participants during cleaning work. Associations between obstructive lung disease and specific cleaning exposures were estimated by unconditional logistic regression models. **(3)** During the second phase, a panel study among 43 current domestic cleaners with respiratory symptoms was also performed. Participants completed a two-week diary including daily information on respiratory symptoms, PEF and cleaning exposures. Mixed models were used to assess the short-term changes in upper and lower respiratory tract symptoms and in PEF in relation to specific cleaning exposures. Individual diagnostic of work-related asthma based on PEF patterns was performed by the Oasys programme and a PEF expert.

Results: In the population-based cross-sectional study, the OR of asthma was 1.46 (95% CI, 1.10 to 1.92) for the 593 (13%) women that were employed in domestic cleaning at the time of the survey, and 2.09 (1.70 to 2.57) for the 1,170 (26%) women that used to be employed in domestic cleaning. Similar results were obtained for chronic bronchitis (OR 1.61 (1.25 to 2.06) and 1.67 (1.37 to 2.02), respectively) and other respiratory symptoms. Current and former work in non-domestic cleaning were not significantly associated with respiratory symptoms. In the case-control study, domestic cleaners with obstructive lung disease were more frequently exposed to bleach and washing dishes than controls (ORs for high versus low frequency of exposure, 4.9 (1.5 to 15) and 3.1 (1.1 to 8.9), respectively). Inhalation accidents involving cleaning products were also more common among cases (OR

2.3 (0.9 to 6.1)). During occupational domestic cleaning activities, airborne chlorine and ammonia were detectable. Although distinction between asthma and chronic bronchitis was difficult, associations were more pronounced for cases with asthma symptoms than for those with symptoms of chronic bronchitis. Atopy was not associated with symptoms of obstructive lung disease. In the panel study, lower respiratory symptoms were more common on working days than on leisure days (OR 4.3 (1.7 to 11)). Presence of these symptoms was predominantly associated with use of diluted bleach (OR 2.5 (1.1 to 5.8)), degreasing sprays/atomizers (2.6 (1.1 to 6.6)) and air refreshing sprays/atomizers (6.5 (2.1 to 20)). Relationships between cleaning exposures and changes in upper respiratory symptoms or PEF were less evident. Thirty percent of the subjects were positively scored for work-related asthma by either Oasys or the expert.

Conclusions: Domestic cleaning women have an increased risk of asthma and chronic bronchitis symptoms. Regular exposure to bleach, and possibly other irritant cleaning agents, is associated with the increased risk of asthma and chronic bronchitis symptoms in this workforce. Transient exposure of those with respiratory disorders to irritant cleaning products is related to the aggravation of lower respiratory symptoms. Mechanisms involved in the induction and/or aggravation of obstructive lung disease in domestic cleaning women are likely to be predominantly irritant-related.

Implications: Our findings may have significant implications for public health, since the use of bleach and other irritant cleaning products is common not only in professional domestic cleaners, but also in other occupations and in the general population, especially among women. Prevention strategies should include informative campaigns about safe handling of irritant cleaning products (including avoidance of inappropriate mixtures), improvement of warning messages in labels and education on other products that can alternatively be used.

1. INTRODUCTION

1.1. Asthma in a Changing Environment

Asthma is a chronic respiratory disease characterized by a variable airflow obstruction in which the affected subjects usually present wheezing, shortness of breath, cough and/or tightness of chest. Asthma is a common disorder affecting approximately between two and twelve percent of people worldwide.[1] Its prevalence varies substantially across the different countries[1,2] and seems to have been increasing during the last decades.[3,4] In addition, recent analyses from the European Community Respiratory Health Survey (ECRHS) have suggested that the incidence of asthma increases progressively by birth cohort.[5]

Because the increase in asthma prevalence has occurred mainly in industrialised countries and over a short period of time, environmental factors rather than genetic factors are suspected to be involved.[6,7] The understanding of asthma aetiology is still incomplete, but risk factors include atopy, parental asthma, gender, occupation, indoor and outdoor air pollution, diet and other lifestyle factors.[8,9] An overall increase in population susceptibility to allergens (i.e., an increase in atopy) has been proposed as a possible explanation for the observed increase in asthma and other allergic diseases in westernised countries.[10] The "hygiene hypothesis" suggests that the lack of early life exposure to microbial agents could alter the immune system in a way that inappropriate (excessive) responses to allergens may occur.[11,12] Less infections in early life are likely to occur in children with no or few siblings, in those not attending the day-care, and in

general in children living in westernised societies. The protective effect of a rural lifestyle[13,14] could be attributed not only to contacts with livestock in childhood,[15-17] but also to a healthier diet,[7,18] a more active lifestyle[9] and a lower exposure to outdoor air pollution.[19,20]

On the other hand, a potential increase in the allergen load has also been postulated as a possible contributor to the global increase of asthma.[6,9] A better insulation of homes in westernised countries could have resulted in higher concentrations of allergens and pollutants associated with asthma in the indoor environment such as house-dust mites,[21] oxides of nitrogen (from gas combustion),[22] or volatile organic compounds.[23] Finally, although genetics cannot account for the global increase in asthma prevalence, the role of gene-environment interactions should not be neglected.[24] Several studies have shown that asthma and atopy have a strong hereditary component and some related genes and genetic regions have already been identified.[25] Individual susceptibility and disease expression are largely determined by genetic factors, and the influence of gene-environment interactions is likely to be of relevance.

1.2. Work-Related Asthma

Occupational asthma has been defined as "asthma due to causes and conditions attributable to a particular occupational environment".[26] However, there is no general consensus about the appropriate use of the term "occupational asthma". Some authors use this term to designate cases of new-onset asthma induced by workplace exposures,[27,28] whereas other authors use it in a broader sense and include also cases of pre-existing asthma exacerbated by workplace exposures.[29,30] As a conciliation of the different points of view, the term "work-related asthma" is

used and includes both new-onset occupational asthma and work-aggravated asthma.[28]

So far, over 350 chemicals, mixtures and processes found in the workplace have been related to asthma in a wide range of occupations.[31] Work-related asthma has become the most common occupational lung disease in many countries and it has been estimated that about 1 in 10 adult asthma cases can be attributed to work.[32] The prevalence of work-related asthma in the general population is difficult to assess but conservative estimates from the ECRHS suggest that about 0.2%-0.5% of young adults have work-related asthma.[33] Although evidence is scarce, several authors have suggested that, in parallel to the increase of asthma in the general population, there has been also an increase in the prevalence and/or incidence of work-related asthma towards the end of the 20th century.[34-37]

1.2.1. Types of Work-Related Asthma

As previously mentioned, work-related asthma includes cases of new-onset occupational asthma as well as cases of work-aggravated asthma. According to the causative mechanism, new-onset occupational asthma can be categorized into two major different types: immunological and non-immunological (see Figure 1).

Immunological occupational asthma, also known as allergic occupational asthma,[28] is characterized by a latency period between beginning of exposure and onset of symptoms.[38] Once an individual is sensitised to an occupational agent, very low concentrations of that specific agent can trigger an asthmatic reaction (i.e., the worker develops specific bronchial hyperresponsiveness).[28] Immunological asthma caused by an IgE-dependent mechanism is predominantly related to high-molecular-weight compounds (≥5 kDa) such as animal and plant proteins but can

also be related to some low-molecular-weight compounds (<5 kDa) such as acid anhydrides and platinum salts.[27] The latter act as haptens and combine with a body protein to form a complete antigen. The specific reaction between antigen and IgE gives rise to an allergic inflammatory reaction in the airways.[27,38] On the other hand, immunological asthma induced by a non-IgE-mediated mechanism is mostly related to low-molecular-weight compounds such as diisocyanates or western red cedar.[39] In this case, the exact immunological mechanisms involved are less well defined.[28]

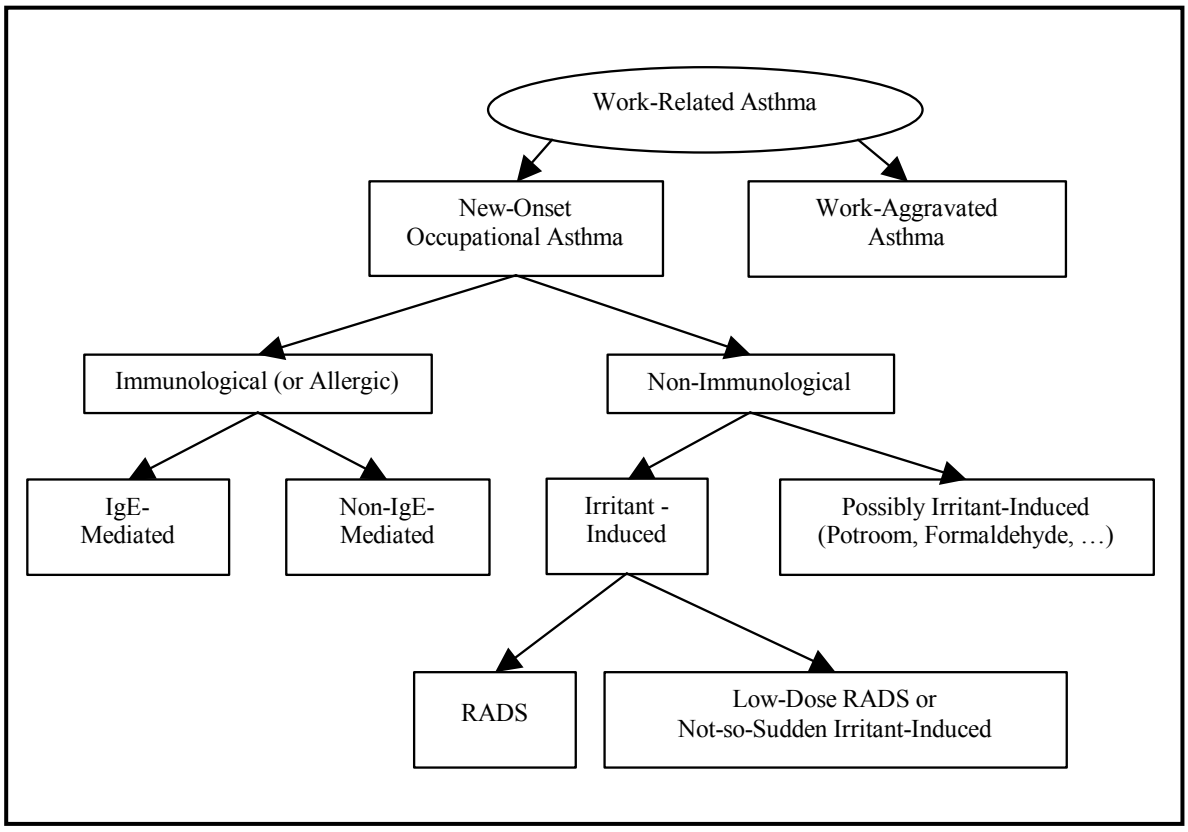

Figure 1. Classification of work-related asthma according to causative mechanism

Non-immunological occupational asthma may or may not occur after a latency period between exposure and onset of symptoms.[39] Subjects with this type of asthma are not sensitised to the inducing agent and they do not manifest specific bronchial hyperresponsiveness.[39,28] Because the agents that induce non-immunological occupational asthma are mostly irritants, this type of asthma is also

known as irritant-induced asthma.[38] However, non-immunological occupational asthma also includes occupational asthma for which induction mechanisms are not yet elucidated, such as aluminium pot-room asthma, meat wrapper's asthma, asthma induced by formaldehyde or asthma induced by machining fluids.[39,40]

The reactive airways dysfunction syndrome (RADS) is the best characterized type of irritant-induced asthma. It was originally described in 1985 as a persistent asthma-like illness occurring after a single high-level exposure to airway irritants with no latency period.[41] Subsequently, the original criteria were modified to include also asthma occurring after high-level exposure to airway irritants on more than one occasion.[42] Airway irritants can be inhaled either as gases or vapours, solid particles or liquid aerosols.[43] Among the large variety of airway irritants that can induce occupational asthma, chlorine and ammonia are the most common.[27,44] Since 1985, RADS has been increasingly reported in the scientific literature and the proportion of RADS among new-onset occupational asthma cases has been estimated to be between 5 and 18%.[45]

Some authors have suggested that recurrent exposure to relatively low levels of respiratory irritants can also induce asthma. In their report of 10 cases, Kipen *et al.* named this type of irritant-induced asthma as "low-dose RADS".[46] Subsequently, Brooks *et al.* described an irritant-induced asthma occurring after repeated and moderate irritant exposures that continued for more than 24 hours but less than four months and termed it as "not-so-sudden irritant-induced asthma".[47]

1.3. Asthma in Cleaning Workers

Cleaning workers were not reported as being at increased risk for asthma until recently. The first epidemiological study reporting an association between cleaning

work and asthma was a population-based case-control study conducted in Singapore.[48] After that, analyses from the Spanish cohort of the ECRHS showed also an increased risk of asthma in cleaning workers[49] and this was subsequently confirmed using data from 26 areas in 12 industrialised countries participating in the ECRHS.[33] In Finland, a study comparing asthma incidence in all employed Finnish females found a relative risk of 1.50 (95% confidence interval (CI), 1.43 to 1.57) for cleaners as compared with administrative workers.[50] More recently, data from the Third National Health and Nutrition Examination Survey in the United States revealed a significant increase in work-related wheezing, and possibly also asthma, among cleaning workers as compared with administrative workers (odds ratio (OR) 5.44 (95% CI, 2.43 to 12.18) and 2.37 (0.53 to 10.58), respectively).[51] In Sweden, however, results from a population-based and a registry-based case-control study showed no increased risks for those ever employed as cleaners.[52,53]

The incidence of work-related asthma in cleaning workers has been estimated from surveillance programmes in the United Kingdom,[54,55] Finland,[56] Sweden,[57] the United States[58] and France.[59] Other countries like Canada (PROPULSE system),[60] South Africa (SORDSA programme)[61] and Italy (PRIOR programme)[62] have also implemented surveillance systems but estimates for cleaning workers have not been provided to date. There are considerable between-country variations in the reported incidence of work-related asthma in cleaners, ranging from 18/million in the United Kingdom to 625/million in California (United States) (Table 1). These differences are probably due not only to the different methods used to estimate incidence rates, but also to between-country differences in occupational exposures within cleaning jobs. In California, cleaners were the occupational group with the highest annual incidence,[58] whereas in the West Midlands (United Kingdom) they represented the group with the lowest incidence.[55] Other small surveillance studies based on hospital registries in Sao Paulo (Brazil)[63] and Cape Town (South Africa)[64] found that cleaning workers were the largest occupational group among work-

related asthma cases (12% and 22%, respectively) and that the most reported agents were cleaning products (20% and 50%, respectively). Estimations of incidence of work-related asthma, however, must be carefully interpreted due to their potential for underestimation, since not all existing cases are seen, diagnosed and reported by a physician, especially in voluntary notification systems.

Table 1. Estimates of annual incidence of work-related asthma in cleaning workers

Country	Surveillance programme	Data collection	Period	Mean annual incidence (/million)		Case definition	Reference
				Cleaners	All occupations		
United Kingdom	SWORD	Voluntary notification by physicians	1989-1997	18	38	New-onset OA	54
United Kingdom (West Midlands)	SHIELD	Voluntary notification by physicians	1990-1997	21	41.2	New-onset OA	55
France	ONAP	Voluntary notification by physicians	1996-1999	55	24	New-onset OA	59
Finland	FROD	Compulsory notification by physicians	1989-1995	80*	180*	New-onset OA	56
Sweden	SRROD	Self-reported	1990-1992	133*	70*	Possible OA (claims for compensation)	57
United States (California)	SENSOR	Compulsory notification by physicians	1993-1996	625	21	New-onset and work-aggravated	58

OA: Occupational asthma. * Incidence in female workers

The evidence for an increased risk of other chronic respiratory diseases in cleaning workers is scarce. Analyses from the ECHRS found a higher risk of chronic bronchitis in non-smoking cleaners without asthma as compared with the group of professional, administrative and clerical workers.[65] A population-based study of elderly women in California found no increased risk of chronic bronchitis for the group of "other service occupations" comprising mainly cleaning workers.[66] Although exposures may vary considerably between different types of cleaning

workers, some of them are substantially exposed to biological and mineral dusts as well as to gases and fumes. These exposures have been related to chronic bronchitis in several occupations[67] and therefore it is conceivable that this could also occur in cleaning workers.

It is increasingly accepted that cleaning work is an occupation at risk for work-related asthma, but little is known about the specific exposures associated with that risk in different types of cleaning workers. Analyses using data from the ECRHS revealed that in Spain domestic cleaning workers were the subgroup of cleaners at a higher risk for asthma.[68] In Finland, a surveillance study among female cleaners found increased asthma risks for non-domestic cleaning workers employed in different industries.[50] The assessment of asthma risk in domestic cleaning workers could not be done in this study because authors were unable to separate those employed in domestic cleaning from other cleaners.

Cleaning workers are exposed to a broad spectrum of cleaning agents in the workplace.[69] The available information about specific cleaning agents related to asthma comes mainly from case reports and surveillance programmes for work-related asthma. Case reports have described the occurrence of asthma as well as other respiratory disorders after single or repeated exposure to a variety of cleaning products. Table 2 shows some selected examples of case reports related to cleaning products in both cleaning and non-cleaning workers. A recent surveillance study in the United States found that unspecified cleaning materials (4.6%), bleach (1.9%) and ammonia (1%), were among the most frequently reported causes of work-related asthma.[85] Similarly, Rosenman *et al.* found that bleach, "acids, bases and oxidizers", unspecified disinfectants, carpet cleaners, floor waxes and ammonia were the most common cleaning products associated with work-related asthma due to cleaning exposures.[86] Interestingly, in this study 78% of cases

associated with cleaning exposures occurred in non-cleaning occupations such as nurses and clerical workers.

Table 2. Case reports of subjects with asthma and other respiratory disorders related to cleaning products

No. of cases	Occupation / activity	Cleaning product	Suspected agent/s	Diagnosis	Country, year	Reference
3	Nurses	Disinfectant solution; surface-cleaning detergent	Benzalkonium chloride	Occupational asthma	France, 2000	70
1	Manufacture of cleaning products	Liquid toilet bowl cleaner	Benzalkonium chloride	Immunological OA	US, 1994	71
1	Pharmacist indirectly exposed	Floor cleaner (Vantropol®)	Benzalkonium chloride	Immunological OA	UK, 1994	72
5	Two cleaning workers, a laboratory and a dispensary technician and a nurse	Disinfectant powder (Halamid®)	Chloramine-T	Immunological OA	The Netherlands, 1981	73
1	Cleaning worker in showers and saunas	Disinfectant (Alinex® solution)	Chloramine-T	Immunological OA	Finland, 1995	74
1	Hospital worker washing surgical tools	Liquid detergent (Klenzyme®)	Proteolytic enzyme (subtilisin)	Immunological OA	Canada, 1996	75
4	Detergent factory workers	Detergent washing powders	Amylase enzyme	Immunological OA	UK, 2000	76
3	Detergent factory workers	Detergent	Cellulase and lipase enzymes	Immunological OA	UK, 2004	77
1	Cleaning worker cleaning floors	Wax-removing detergent	Ethanolamine	Immunological OA	Finland, 1994	78
1	Washroom cleaning	Sulphuric acid	Sulphuric acid	RADS	Canada, 1988	79
1	Pool cleaning	Hydrochloric acid	Hydrochloric acid	RADS	Canada, 1988	79
1	Household cleaning (toilet)	Whink Rust Remover®	Hydrofluoric acid	RADS	US, 2003	80
1	Cleaning worker in a hospital kitchen	Ammonia; alkaline detergent (Duromax-4®)	Ammonia; concentrated bases	Low-dose RADS	Spain, 2000	81
1	Cleaning worker of industrial jam containers	Lye (sodium hydroxide solution)	Sodium hydroxide	Obstructive airway disease	Israel, 1992	82
1	Household cleaning (bathtub)	Whink Rust Remover®	Hydrofluoric acid	Chemical pneumonitis and ARDS	US, 1997	83
1	Hospital worker washing surgical tools	Liquid detergent (Klenzyme®)	Proteolytic enzyme (subtilisin)	Extrinsic allergic alveolitis	US, 2001	84

OA: Occupational Asthma. RADS: Reactive Airways Dysfunction Syndrome. ARDS: Adult Respiratory Distress Syndrome

Massive exposure to highly irritant fumes coming from inadequate mixtures of cleaning agents is also relatively common in cleaning workers, as well as in other occupations and in the general population.[86,87] Reilly *et al.* reported that mixing of cleaning products accounted for 10% and 13% of hospitalisations for inhalation accidents in the workplace and outside the workplace, respectively.[87] In this study, a non-negligible part of the inhalation accidents also occurred when using a single cleaning product (6% and 11%, respectively). Inhalation accidents involving mixtures of cleaning agents have been related to several respiratory disorders, including RADS.[88,89] According to data from poison control centres and surveillance systems in the United States, most of cleaning inhalation accidents involve the mixture of bleach (sodium hypochlorite) with other cleaning products.[86,90,91] This becomes also evident when reviewing case series reported in the literature (Table 3). Mixing bleach either with ammonia or with acids releases large amounts of the strongly irritant gases chloramine and chlorine, respectively.[101] One of the largest case series of RADS after mixture of bleach with hydrochloric acid appeared very recently in Turkey, where this combination of cleaning agents is commonly used by housewives.[89]

The mechanisms involved in the induction or aggravation of asthma in cleaning workers can be related to either sensitising or irritant exposures. Volatile organic compounds, which are believed to induce and/or aggravate asthma,[102] are emitted when using cleaning agents. About 100 volatile organic compounds, including both sensitising and irritant agents, have been identified in cleaning products.[69] The most common sensitising substances in cleaning products include perfumes or fragrances, such as pinene[103] or limonene,[104] preservatives such as isothiazolinones or formaldehyde,[105] disinfectant substances such as chloramine-T[73,74] or benzalkonium chloride[71,72] and detergent enzymes[106,107,108] such as proteases, amylases or cellulases. In addition, some cleaning tasks such as dusting or sweeping involve exposure to house-dust mite and other indoor allergens

susceptible to induce sensitisation and asthma in sensitised individuals.[109] On the other hand, cleaning workers are also exposed to a wide range of irritant cleaning agents, including among others ammonia, hydrochloric acid, acetic acid, sodium hypochlorite and sodium hydroxide. As previously mentioned, regular exposure to these and other irritant cleaning products could result in low-dose RADS, whereas a massive exposure due to improper use or inadequate mixture with other cleaning products can result in RADS. In fact, cleaning materials were the most frequently reported agents associated with work-related RADS in a surveillance study in the United States.[45]

Table 3. Case reports of subjects with asthma and other respiratory disorders related to mixtures of cleaning products

No. of cases	Occupation / activity	Mixture	Suspected agent/s	Diagnosis	Country, year	Reference
1	Household cleaning	Sodium hypochlorite and hydrochloric acid	Chlorine	RADS	France, 1994	88
55	Household cleaning	Sodium hypochlorite and hydrochloric acid	Chlorine	RADS	Turkey, 2004	89
1	Household cleaning (bathroom)	Sodium hypochlorite and ammonia	Chloramine	Pneumonitis	Israel, 1982	92
3	Household cleaning	Sodium hypochlorite and ammonia	Chloramine	Pneumonitis	US, 1986	93
1	Cleaning a walk-in freezer at work	Sodium hypochlorite and ammonia	Chloramine	Pneumonitis	US, 1999	94
72	Soldiers cleaning their barracks	Sodium hypochlorite and ammonia	Chloramine	Diverse respiratory complaints	US, 1998	95
14	Psychiatric patients performing cleaning duties as therapy	Sodium hypochlorite and phosphoric acid	Chlorine	Diverse respiratory complaints	US, 1991	96
2	Household cleaning (aquarium)	Sodium hypochlorite and hydrochloric acid	Chlorine	Pneumomediastinum	Israel, 1982	97
1	Cleaning worker cleaning a shower	Sodium hypochlorite and a detergent containing acids	Chlorine	Severe asthma attack and ARDS	Italy, 2000	98
1	Household cleaning (bathtub)	Sodium hypochlorite (Clorox®) and sodium bisulfate (Sani-Flush®)	Chlorine	Pulmonary oedema	US, 1972	99
1	Household cleaning (unstopping a kitchen drain)	Drain-cleansing agents (Plum-R®, Drano®, Clorox®, Sani-Flush®)	Chlorine and chlorides	Severe airway obstruction	US, 1976	100

RADS: Reactive Airways Dysfunction Syndrome. ARDS: Adult Respiratory Distress Syndrome

To date, the only epidemiological study that has analysed the association between specific cleaning exposures and asthma in cleaning workers (particularly, in domestic cleaning workers) was performed within the Spanish cohort of the ECRHS.[68] According to this study, the highest asthma risks were associated with cleaning kitchens and using furniture sprays and oven sprays. However, this study was not designed to assess associations with specific cleaning exposures, resulting in a small and selected population along with the possible influence of recall bias.

2. RATIONALE

The epidemiological evidence for an increased risk of asthma in cleaning workers, and specifically in domestic cleaning workers, was very scarce when we initiated the EPIASLI study (Epidemiological Study of the Risk of Asthma in Cleaning Workers). Few years before, our research group had reported an association between cleaning work and asthma in the Spanish cohort of the ECRHS,[49] confirming later these results with data from all the participating countries.[33] Subsequently, analyses within the Spanish cohort of the ECRHS[68] evaluated the specific exposures associated with asthma in cleaning workers and suggested an increased risk for domestic cleaning workers. Based on these results, we decided to initiate the EPIASLI study, designed in first instance to substantiate the excess risk of asthma in domestic cleaning workers and, if confirmed, to examine the specific occupational risk factors.

The undeclared nature of the domestic cleaning occupation and the consequent lack of registries led us to conduct the study in two phases. In the first phase, we carried out a cross-sectional study among 4,521 women living in a city with a known high proportion of women employed in domestic cleaning. From this study, we identified 650 women that reported active employment in domestic cleaning at the time of the study. This allowed us to conduct, in a second phase, a nested case-control study and a panel study to identify which particular tasks and products were related to respiratory symptoms in domestic cleaning women.

The importance of the EPIASLI study lays in the fact that it is the first epidemiological study specifically designed to assess in detail the occupational risk factors for asthma symptoms in domestic cleaning workers. Findings from this study will contribute to establish the basis for the development of preventive measures in cleaning workers, which could also be relevant for housewives and other people performing cleaning tasks at home.

3. OBJECTIVES

3.1. Objectives of the Population-Based Cross-Sectional Study:

Main Objectives:

Assess the risk of asthma symptoms in domestic and non-domestic cleaning women.

Identify a cohort of domestic cleaning women suitable to carry out a case-control study.

Secondary Objectives:

Assess the risk of other respiratory symptoms in domestic and non-domestic cleaning women.

Assess the risk of asthma and other respiratory symptoms associated to former cleaning work.

3.2. Objectives of the Case-Control Study

Describe the exposure pattern of domestic cleaning women.

Identify the specific cleaning tasks and products associated with a higher risk of asthma and chronic bronchitis* symptoms in domestic cleaning women.

Identify the clinical features of cleaning-related asthma and elucidate the immunological or irritant mechanisms involved by considering the cleaning tasks and products implicated.

Provide information for the establishment of preventive measures to protect the respiratory health of domestic cleaning workers.

3.3. Objectives of the Panel Study

Assess the relationship between specific cleaning exposures and short-term changes in respiratory symptoms and peak expiratory flow among domestic cleaning women with asthma and/or chronic bronchitis* symptoms.

Elucidate the immunological or irritant mechanisms involved in the potentially observed short-term changes in respiratory symptoms and peak expiratory flow.

Provide information for the establishment of preventive measures to protect the respiratory health of domestic cleaning workers.

* Due to the results obtained in the population-based survey, the initial objectives were expanded to include also chronic bronchitis as outcome of interest.

4. PAPER # 1

Asthma Symptoms in Women Employed in Domestic Cleaning: a Community Based Study*

* Medina-Ramón M, Zock JP, Kogevinas M, Sunyer J, Antó JM. Asthma symptoms in women employed in domestic cleaning: a community based study. **Thorax** 2003;58:950-954.

ABSTRACT

Background

Epidemiological studies have shown an association between cleaning work and asthma, but the risk factors involved are not clear. One small study suggested that asthma in cleaners was predominantly related to domestic cleaning work. We aimed to study the risk of asthma in women employed in domestic cleaning.

Methods

We conducted a cross-sectional study in 4,521 Spanish women with low educational level, aged 30 to 65 years. Information on respiratory symptoms and cleaning work history was obtained using a postal questionnaire with telephone follow-up. Asthma was defined as reported symptoms in the last year or current use of asthma medication. Odds ratios (ORs) with 95% confidence intervals (CIs) for asthma in different cleaning groups were estimated using adjusted unconditional logistic regression models.

Results

593 women (13%) were currently employed in domestic cleaning work. Asthma was more prevalent in this group than in women who had never worked in cleaning (OR 1.46 (95% CI, 1.10 to 1.92)). Former domestic cleaning work was reported by 1170 women (26%), and was strongly associated with asthma (OR 2.09 (1.70 to 2.57)). Current and former non-domestic cleaning work was not significantly associated with asthma. Consistent results were obtained for other respiratory symptoms. 25% of the asthma cases in the study population were attributable to domestic cleaning work.

Conclusions

Employment in domestic cleaning may induce or aggravate asthma. Our study indicates a considerable public health impact related to domestic cleaning work, probably including not only professionals but also people performing cleaning tasks at home.

Key words

Epidemiology, occupation, asthma, respiratory, cleaning.

INTRODUCTION

Asthma is the most common occupational lung disease in industrialised countries.[38] Occupational exposures are estimated to be responsible for 5 to 20% of all adult asthma cases[32] and numerous occupations with increased risk and causative agents have been identified.[110] Several community-based studies have recently shown an increased risk for asthma in cleaners, an occupation not traditionally associated with this disease. [33, 111] However, the types of exposure associated with asthma in cleaners have not been identified. Analyses within the Spanish centres of the European Community Respiratory Health Survey (ECRHS) suggested that the excess risk for asthma in cleaners occurred mostly in domestic cleaners.[68] Results of this study, however, were based on a small and selected population sample, and the possible influence of recall bias could not be excluded. No other study has been published assessing the association between employment in domestic cleaning and asthma. If confirmed, an increased risk of asthma in domestic cleaners could be of substantial public health importance since this is a large occupational group and some of their exposures are shared by housewives and other people performing cleaning tasks at home. Studying domestic cleaners is particularly difficult given the informal nature of this occupation in many

countries and the lack of available registries. We carried out a large cross-sectional study in a population with an expected high number of domestic cleaners, aiming at assessing the risk of asthma in this workforce.

METHODS

A cross-sectional study was conducted in Cornellà, a city in the metropolitan area of Barcelona, Spain. All female residents between 30 and 65 years of age and with less than eight years of education were identified using the municipal census, and a random sample of 5,390 women (37%) was taken from this selected population. Errors in addresses or in registered age resulted in 270 non-eligible subjects.

Between June 2000 and July 2001 a short questionnaire was sent by mail to all 5,120 eligible subjects. Telephone follow-up was performed for those who did not respond by mail or had important missing data in the postal questionnaire. The participants were not informed about the main study hypothesis (i.e., the association between domestic cleaning and asthma).

The questionnaire included symptom questions extracted from the questionnaire used in the ECRHS.[112] The validity and reliability of these questions have been described elsewhere.[113] Participants were asked whether they had experienced: (a) wheezing with breathlessness in the last 12 months; (b) wheezing apart from colds in the last 12 months; (c) ever having had asthma and, if affirmative, the age of the first asthma attack; (d) being woken by an attack of shortness of breath in the last 12 months; (e) having had an attack of asthma in the last 12 months; (f) current use of medication for asthma; (g) regular cough at least 3 months each year; (h) regularly bringing up phlegm at least 3 months each year; (i) ever having had a problem with sneezing or a runny or a blocked nose when not having a cold or the

flu; (j) ever having had respiratory problems due to any job and, if affirmative, having quit that job. *Current asthma* was defined as an affirmative answer to at least one of the questions (d), (e) or (f) .[33] *Adult-onset asthma* was defined as an affirmative answer to (c) with the first attack of asthma at age of 15 years or older. *Chronic bronchitis* was defined as a positive answer to questions (g) or (h). *Ever rhinitis* was defined as a positive answer to question (i). *Work-related respiratory symptoms* were defined as an affirmative answer to question (j).

Detailed questions about history in cleaning work followed the respiratory symptom questions. Subjects were classified according to timing and type of cleaning work. We distinguished between current (at the time of the interview) and former cleaning work. All women who were paid to clean somebody else's home (including those paid on an hourly or an *ad hoc* basis) were considered to be domestic cleaners. Other paid cleaning workers were regarded as non-domestic cleaners. Women who worked simultaneously in domestic and non-domestic cleaning were included in the domestic cleaning group. Detailed information about the site of non-domestic cleaning work was only requested in current non-domestic cleaners.

Statistical analyses were done using Stata version 6.0 (Stata Corporation, College Station, Texas, USA). Unconditional logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for each cleaning group and respiratory outcome. All ORs were adjusted for age group and smoking status. Women who had never worked in cleaning were used as the reference group.

RESULTS

Of the eligible sample of 5,120 women, questionnaire data were obtained for 4,592 subjects (response rate 90%). No major differences in age or educational level were observed between responders and non-responders. After excluding those with missing data, final analyses were done with 4,521 subjects. The mean age of the women in the study population was 50.7 (SD 9.4) years and most of them had never smoked (Table 1). Half of the population had at some time been employed in cleaning. Among these, 39% were working as cleaners at the time of the interview, most of them in private home cleaning. A minority of the current domestic cleaning women (14%) worked simultaneously as cleaners in a non-domestic site. The large majority (85%) of the 1,371 former cleaning women had been working in domestic cleaning.

The prevalence rate of current asthma and chronic bronchitis in the study population was 12.6% and 15.2%, respectively (Table 2). Six per cent reported ever having had asthma, and 74% of them had their first asthma attack at the age of 15 years or older.

Those reporting ever having worked as cleaners showed an excess risk for all respiratory outcomes under study in comparison with those who had never worked as cleaners (Table 3). Risks in former cleaners were slightly higher than in current cleaners. Domestic cleaning was consistently associated with all respiratory symptoms. Increased risks of both current asthma and chronic bronchitis were observed in current domestic cleaners (OR 1.46d (95% CI, 1.10 to 1.92) and 1.61 (1.25 to 2.06), respectively) and in former domestic cleaners (OR 2.09 (1.70 to 2.57) and 1.67 (1.37 to 2.02), respectively). Non-domestic cleaners did not show any statistically significant risk, although for some symptoms non-significantly increased risks were observed in former non-domestic cleaners. The same pattern

was observed for all other respiratory symptoms not shown in Table 3. When analyses were repeated defining chronic bronchitis as both regular cough and phlegm, the odds ratios were very similar. Furthermore, when subjects reporting simultaneously asthma and chronic bronchitis were excluded from analyses, asthma and chronic bronchitis risks did not change substantially. Additional adjustment for educational level yielded essentially similar risk estimates as those presented in Table 3.

The prevalence rate of work-related respiratory symptoms was 12% for women who had ever worked as cleaners, and 5% for women who had never worked in cleaning (results not shown). The proportion of former cleaners reporting having quit the cleaning job due to work-related symptoms was 1.3%. When analyses were repeated excluding those who had quit any job due to respiratory problems, former cleaners still presented a higher risk for asthma (OR 1.83 (95% CI, 1.48 to 2.26)) than current cleaners (OR 1.35 (1.04 to 1.74)).

Current asthma and chronic bronchitis risks in current domestic cleaners were stratified by potential effect-modifiers (Table 4). The risk of chronic bronchitis was significantly higher for smokers as compared to non-smokers (interaction $p<0.05$). Both asthma and chronic bronchitis risks decreased with increasing age, the difference between the lower and the upper age tertile being statistically significant for asthma. Cleaners who worked simultaneously in domestic and non-domestic cleaning had a significantly ($p<0.05$) higher asthma risk (OR 2.79 (95% CI, 1.64 to 4.75)) than those who were exclusively employed in domestic cleaning (OR 1.26 (0.93 to 1.71)).

Current non-domestic cleaners worked in a wide variety of locations (Table 5). The largest category comprising office cleaners did not show an excess risk, neither for asthma nor for chronic bronchitis. A statistically significant risk for asthma and

chronic bronchitis was observed in subjects cleaning in hospitals and other health care centres. Non-significant asthma risks were observed in cleaners working in hotels and residences, laboratories, and kitchens.

DISCUSSION

This community-based study is the first epidemiological investigation specifically designed to assess the risk of asthma in women employed as domestic cleaners. Significantly elevated risks for asthma and other respiratory symptoms were found in women currently working as domestic cleaners, as well as in women who had a domestic cleaning job in the past.

The increased asthma risk observed in current domestic cleaners confirms the results obtained in an analysis of a small sub-sample of the ECRHS.[68] Consistently, several surveillance programmes[58,85,114] and case reports[71,72,81] have suggested that exposure to cleaning products is associated with work-related asthma in numerous occupations, although no specific reference has been made to domestic cleaning. The observed high prevalence of asthma in current domestic cleaners could be a consequence of either a net increase of incidence among domestic cleaners or a longer duration of a pre-existing asthma. In both situations the occupational exposure is equally relevant as it is well recognized that work-related asthma includes both types of cases. With the present data we cannot distinguish between these two different patterns of work-related asthma. Domestic cleaning workers are exposed to a large variety of cleaning products containing both irritants and sensitizers as well as to indoor allergens.[69] Consequently, it can be hypothesized that the onset or aggravation of asthma in domestic cleaners could be related to an irritant-induced mechanism or to specific sensitisation.

Former cleaners showed a higher asthma risk than current cleaners. A possible explanation for this finding could be the healthy worker effect. Namely, those who get the disease are more likely to leave the job, resulting in an increase of the asthma prevalence in former cleaners and a decrease in current cleaners. This is supported by the fact that the majority of occupational asthma cases fail to recover after removal from exposure.[115] However, in our study, the percentage of former cleaners that reported having quit the cleaning job due to respiratory problems was relatively low (1.3%). When analyses were repeated excluding subjects that had quit a job due to respiratory problems, former cleaners still presented a higher asthma risk than current cleaners. Therefore, apart from the healthy worker effect, there are probably other determinants responsible for the difference in asthma risks between former and current cleaners. It can be hypothesized that relevant exposures in cleaners have decreased during the last decades, as also observed in other jobs,[116] leading to a different exposure pattern between current and former cleaners.

Taking into consideration the prevalence of women who have ever worked in domestic cleaning (13.1% in the present and 25.9% in the past) and the associated asthma risk, it can be estimated that about 25% of the asthma cases in our study population could be attributed to having a history of domestic cleaning work. This large figure has probably been influenced both by the characteristics of the area where the study population was recruited (an industrial city within a large metropolitan area) and by the sampling scheme. The proportion of domestic cleaning women in the general population is difficult to estimate given that in most cases domestic cleaning constitutes an informal occupation in which women are self-employed and no registries are available. In the Spanish population of the ECRHS, 2% of the female participants were current domestic cleaners, representing one-third of all current cleaners. Using recent data from the National Institute of Statistics in Spain we estimated that approximately 10% of women over 16 years

old worked in cleaning in 2000. Cleaning work is probably also a common occupation among women in other countries. According to a recent study, about 5% of employed Finnish women work in non-domestic cleaning.[50] In addition, our findings for domestic cleaning might also have implications for people performing cleaning tasks in their own homes. Several studies have found significantly increased risks for asthma and chronic bronchitis in housewives[33,66,117] and it has been estimated that 5% of the asthma risk among women could be attributed to household exposures.[33] In addition, Reilly and Rosenman[87] and Jajosky[85] showed that exposure to household cleaning agents was among the most frequent environmental causes of non-work-related hospital admissions for asthma.

Our results show that working or having worked as a domestic cleaner was also associated with several respiratory symptoms other than asthma, including chronic bronchitis. The association between domestic cleaning work and chronic bronchitis remained statistically significant in non-smokers, indicating that confounding by smoking did not play an important role. In addition, non-asthmatic domestic cleaners showed a significantly increased risk of bronchitis, suggesting that asthma and chronic bronchitis were independent outcomes. Our findings are in agreement with results of a study in which asthmatic cleaners showed a significantly higher prevalence of chronic bronchitis than asthmatic office workers.[118]

The association between non-domestic cleaning work and asthma was not clear. The different risk of asthma observed in domestic and non-domestic cleaning workers could be related to qualitative or quantitative differences in the cleaning exposures of both groups. Since non-domestic cleaners worked in a wide variety of different locations, risks were assessed separately for each location. A high asthma risk was found for cleaners in several locations, but estimates were based on small numbers. Only hospital cleaners showed a statistically significant asthma risk, which could partly be due to shared exposures related to asthma in nurses such as

latex, disinfectants and sensitising drugs. This is consistent with findings of a Finish surveillance study that also found an increased asthma risk for cleaners working in health and social work centres.[50] A general conclusion from this study was that part of the increased asthma risk observed in several types of non-domestic cleaning workers was due to exposures inherent to the environment where cleaning work was performed.

There are several limitations in our study that should be considered. The study population of our survey was restricted to female subjects in view of the fact that the large majority of domestic cleaning workers in Spain are women.[68] Furthermore, we cannot exclude the possibility of misclassification of occupational group, mainly due to two circumstances. Firstly, many cleaning workers change their place of work frequently and those employed in domestic cleaning tend to show intermittence in their employment. Secondly, it is possible that some domestic cleaning workers did not report their occupation as a result of the informal status of this job. Nevertheless, it can be expected that misclassification was non-differential, which is likely to produce bias towards the null rather than false positive associations.[119]

In conclusion, employment in domestic cleaning was found to be associated with asthma, chronic bronchitis and other respiratory symptoms among Spanish women. These findings are supported by results from several surveillance studies and case reports. The high risk of asthma attributable to domestic cleaning indicates a substantial public health impact, which might be even greater if we take into consideration that housewives and others doing cleaning tasks at home are probably also at risk. Further research is needed to identify the specific exposures responsible for the increased asthma risk in domestic cleaners.

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Table 1. Characteristics of the study population (N=4,521)

		n	%
Age	30-39 years	702	15.5
Age	40-49 years	1,150	25.4
Age	50-59 years	1,750	38.7
Age	60-65 years	919	20.3
Never smoked		3,355	74.2
Ex-smokers		319	7.1
Current smokers		847	18.7
Never worked in cleaning		2,262	50.0
Current domestic cleaners*		593	13.1
Current non-domestic cleaners†		295	6.5
Former domestic cleaners		1,170	25.9
Former non-domestic cleaners		201	4.4

* 85 subjects in this category were employed both in domestic and non-domestic cleaning. † 120 subjects in this category had been domestic cleaners in the past.

Table 2. Prevalence of respiratory symptoms (N=4,521)

Symptoms	n*	%
Wheezing in the last 12 months	819	18.1
Wheezing with breathlessness	503	11.1
Wheezing apart from colds	422	9.3
Ever asthma	270	6.0
Childhood-onset asthma†	43	1.0
Adult-onset asthma‡	199	4.4
Current asthma §	568	12.6
Being woken by an attack of shortness of breath in the last 12 months	491	10.9
Attack of asthma in the last 12 months	107	2.4
Current use of medication for asthma	152	3.4
Chronic bronchitis ‖	685	15.2
Regular cough at least three months each year	468	10.4
Regularly bringing up phlegm at least three months each year	398	8.8
Both the above symptoms	181	4.0
Ever rhinitis	1,628	36.0
Work-related symptoms¶	389	8.6

* Missing data for specific symptoms between 0 and 42 subjects. † First attack of asthma at age <15 years. ‡ First attack of asthma at age 15 years or older. § Woken by an attack of shortness of breath in the last 12 months, or attack of asthma in the last 12 months, or current use of medication for asthma. ‖ Regular cough at least three months each year, or regularly bringing up phlegm at least three months each year. ¶ Respiratory problems caused by any job.

Table 3. Association between type and timing of cleaning work and selected respiratory symptoms

	Wheezing with breathlessness	Ever asthma	Current asthma*	Chronic bronchitis†	Ever rhinitis
Ever worked in cleaning	1.53 (1.27 to 1.85)	1.44 (1.12 to 1.85)	1.73 (1.44 to 2.07)	1.52 (1.29 to 1.80)	1.20 (1.06 to 1.35)
Current cleaner	1.37 (1.06 to 1.76)	1.03 (0.72 to 1.47)	1.32 (1.04 to 1.69)	1.41 (1.13 to 1.76)	1.08 (0.92 to 1.28)
Domestic	1.48 (1.11 to 1.97)	1.21 (0.82 to 1.79)	1.46 (1.10 to 1.92)	1.61 (1.25 to 2.06)	1.18 (0.97 - 1.42)
Non-domestic	1.17 (0.79 to 1.76)	0.68 (0.35 to 1.32)	1.08 (0.72 to 1.61)	1.08 (0.76 to 1.55)	0.92 (0.71 to 1.20)
Former cleaner	1.63 (1.32 to 2.02)	1.68 (1.28 to 2.21)	2.00 (1.63 to 2.43)	1.58 (1.31 to 1.90)	1.27 (1.12 to 1.47)
Domestic	1.69 (1.35 to 2.10)	1.76 (1.33 to 2.33)	2.09 (1.70 to 2.57)	1.67 (1.37 to 2.02)	1.31 (1.13 to 1.51)
Non-domestic	1.34 (0.85 to 2.11)	1.22 (0.66 to 2.26)	1.41 (0.91 to 2.18)	1.09 (0.71 to 1.66)	1.11 (0.82 to 1.50)

Odds ratios (95% confidence intervals) relative to those who had never worked in cleaning (n=2,262), adjusted for age category and smoking status.
* Woken by an attack of shortness of breath in the last 12 months, or attack of asthma in the last 12 months, or current use of medication for asthma.
† Regular cough at least three months each year, or regularly bringing up phlegm at least three months each year.

Table 4. Association between current domestic cleaning, current asthma and bronchitis, stratified by smoking status, age category and employment in another cleaning job

	Never cleaners (n)	Current domestic cleaners (n)	Current asthma*	Chronic bronchitis†
Current non-smokers	1,843	484	1.50 (1.11 to 2.04)	1.37 (1.02 to 1.85)
Current smokers	419	109	1.27 (0.65 to 2.46)	2.40 (1.52 to 3.80)‡
Age 30 – 46 years	733	199	1.96 (1.22 to 3.13)	1.85 (1.25 to 2.74)
Age 47 – 55 years	746	243	1.46 (0.94 to 2.27)	1.57 (1.02 to 2.41)
Age 56 – 65 years	783	151	1.00 (0.57 to 1.76)§	1.35 (0.83 to 2.20)
Exclusively domestic cleaning	2,262	508	1.26 (0.93 to 1.71)	1.55 (1.19 to 2.02)
Domestic and non-domestic cleaning simultaneously	2,262	85	2.79 (1.64 to 4.75)‖	1.93 (1.13 to 3.29)

Odds ratios (95% confidence intervals) relative to those who had never worked in cleaning. * Woken by an attack of shortness of breath in the last 12 months, or attack of asthma in the last 12 months, or current use of medication for asthma. † Regular cough at least three months each year, or regularly bringing up phlegm at least three months each year. ‡ Different from risk in non-smokers; $p<0.05$ for multiplicative interaction. § Different from risk in age group 30–46 years; $p<0.1$ for multiplicative interaction. ‖ Different from risk in exclusively domestic cleaners ($p<0.05$).

Table 5. Association between location of non-domestic cleaning work, current asthma and chronic bronchitis

Location of cleaning work*	n	Current asthma†	Chronic bronchitis‡
Offices	124	1.0 (0.6 to 1.9)	0.9 (0.5 to 1.5)
Schools and other educational centres	53	0.6 (0.2 to 1.8)	1.1 (0.5 to 2.4)
Hospitals and other health care centres	34	2.5 (1.1 to5.8)	2.2 (1.0 to 4.8)
Shops and public buildings	26	0.4 (0.1 to 3.0)	0.6 (0.2 to 2.8)
Factories	19	1.2 (0.3 to 5.0)	0.9 (0.2 to 3.8)
Hotels and residences	18	1.9 (0.5 to6.6)	1.9 (0.6 to 6.0)
Bars and restaurants	13	0 (-)	1.3 (0.3 to 5.8)
Flat entrances and staircases	9	1.3 (0.2 to 10.5)	1.9 (0.4 to 9.7)
Kitchens	6	2.1 (0.2 to 17.6)	3.8 (0.7 to 21.1)
Sports installations	6	0 (-)	1.7 (0.2 to 14.9)
Laboratories	6	1.9 (0.2 to 16.7)	1.1 (0.1 to 9.4)
Other locations	8	0 (-)	0.9 (0.1 to 7.5)

Odds ratios (95% confidence intervals) relative to those who had never worked in cleaning (n=2,262), adjusted for age category and smoking status. * Subjects may appear in more than one category. † Woken by an attack of shortness of breath in the last 12 months, or attack of asthma in the last 12 months, or current use of medication for asthma. ‡ Regular cough at least three months each year, or regularly bringing up phlegm at least three months each year.

5. PAPER # 2

Asthma, Chronic Bronchitis and Exposure to Irritant Agents in Occupational Domestic Cleaning: a Nested Case-Control study*

* Medina-Ramon M, Zock JP, Kogevinas M, Sunyer J, Torralba Y, Borrell A, Burgos F, Antó JM Asthma, chronic bronquitis and exposure to irritant agents in occupational domestic cleaning: a Nested case-control study. **Occupational and Environmental Medicine** 2005 62 (9): 598-606

ABSTRACT

Objectives

Women employed in domestic cleaning are at an increased risk for symptoms of obstructive lung disease, but the responsible exposures are unknown. We investigated common tasks and products in occupational domestic cleaning in relation to respiratory morbidity.

Methods

We conducted a case-control study in domestic cleaning women nested within a large population-based survey of women aged 30 to 65 years. We identified 160 domestic cleaning women with asthma symptoms, chronic bronchitis symptoms, or both and 386 without a history of respiratory symptoms. We further evaluated detailed exposures for 40 cases that reported still having symptoms at the recruitment interview, and 155 controls that reported again not having symptoms. All tasks performed and products used when cleaning houses were obtained in a face-to-face interview. Lung function, methacholine challenge and serum IgE testing were also performed. Personal exposure measurements of airborne chlorine and ammonia were performed in a subsample. Associations between asthma, chronic bronchitis and cleaning exposures were evaluated using multiple logistic regression analysis.

Results

Airborne chlorine (median level 0 to 0.4 ppm) and ammonia (0.6 to 6.4 ppm) were detectable during occupational domestic cleaning activities. Cases used bleach more frequently than controls; adjusted Odds Ratio (OR) for intermediate exposure was 3.3 (95% confidence interval, 0.9 to 11) and for high exposure 4.9 (1.5 to 15). Other independent associations included accidental inhalation of vapours and gases from cleaning agents and washing dishes. These associations were more

pronounced for cases with asthma symptoms than for those with symptoms of chronic bronchitis, but were not related to sensitisation to common allergens.

Conclusions

Asthma symptoms in domestic cleaning women are associated with exposure to bleach and possibly other irritant agents. The public health impact of the use of irritant cleaning products could be widespread since the use of these products is common both in the workplace and at home.

Key words

Asthma, occupation, cleaning, irritants

INTRODUCTION

Community-based studies have shown that cleaning workers have an increased risk for asthma and other respiratory symptoms,[33,48,51,111] but the responsible exposures remain unclear. Recent studies have demonstrated a particularly high risk of respiratory morbidity in women employed in domestic cleaning.[68,120] In a large cross-sectional study we previously showed that women employed in domestic cleaning had an excess risk of both asthma and chronic bronchitis symptoms.[120] In this general population sample of women aged 30 to 65 years, the risk of asthma attributable to employment in domestic cleaning was about 25%. To our knowledge, to date no study has been published evaluating specific risk factors for asthma or chronic bronchitis in domestic cleaning workers. This is a potentially important public health issue since domestic cleaning is one of the most common female occupations in many countries, and relevant exposures are shared by housewives and others cleaning their own homes.[33,68,120] Here we report the results of a population-based nested case-control study among women employed in

domestic cleaning, aiming at identifying which exposures in occupational domestic cleaning are related to asthma and chronic bronchitis symptoms.

METHODS

Study Design and Population

Between June 2000 and July 2001 a population-based survey was conducted among 4,521 women between 30 and 65 years of age living in Cornellà, a city in the metropolitan area of Barcelona, Spain.[120] Within this study population, a nested case-control study among domestic cleaning women was performed between June 2001 and April 2002. Because symptoms of asthma typically show variable patterns in time,[121] case-control status was determined on the basis of the presence or absence of respiratory symptoms at the time of both studies. Cases were defined as women with asthma and/or chronic bronchitis both at the population-based survey and at the case-control study. Asthma was defined as having had an attack of asthma and/or being woken by an attack of shortness of breath in the last 12 months, and chronic bronchitis was defined as having regular cough and/or regularly bringing up phlegm at least three months each year. Controls were defined as women who reported not having experienced respiratory symptoms in the preceding year and did not have a history of asthma at both the population-based interview and the case-control interview.

From the population-based survey 650 women currently employed in domestic cleaning work were identified, among whom 160 had asthma and/or chronic bronchitis symptoms, and 386 were without respiratory symptoms (Figure 1). Both groups were contacted again, and those who were still employed in domestic cleaning and living in the study area were invited to participate in the case-control study. Eighty-seven women who had reported asthma symptoms, chronic

bronchitis symptoms, or both at the population-based survey (response rate 74%) and 194 women without respiratory symptoms (69%) agreed to participate. There were no major differences in age (median 51 vs. 53 years), smoking (15% vs. 13% current smokers) and educational level (46% vs. 43% at least primary education) between responders and non-responders. There were relatively more participant cases who were also employed in non-domestic cleaning compared to participant controls. Since change in symptom status between the population-based survey and the case-control recruitment was common in both groups, we defined case-control status according to the presence or absence of symptoms at both occasions, resulting in 40 cases and 155 controls. The study protocol was approved by the local institutional committee on ethical practice, and participants provided written informed consent.

Exposure Assessment

Detailed information about history of employment and characteristics of current domestic cleaning work was obtained during the case-control study. A questionnaire was developed based on a previous study in Spanish cleaners[68] and on a job-specific questionnaire used within the European Community Respiratory Health Survey (ECRHS),[122] and revised after a pilot study. Subjects were asked about specific cleaning characteristics separately for each home where currently employed, and their own home. The frequency of performance of 23 different cleaning tasks and use of 22 different cleaning products at the time of the case-control interview was recorded as either times per week, times per month or times per year. All frequencies were converted into times per year and exposures in all homes, including their own, were summed to obtain a total frequency of exposure to each task and each product. Questions about accidents that occurred when using a single or mixing several cleaning products leading to the inhalation of an important quantity of vapours, gas or fumes were also included. Full occupational history was obtained, and exposure to asthma-related agents in all jobs was

assessed by means of a job-exposure matrix with additional expert judgement.[123] The questionnaire was administered face-to-face by a trained research nurse, blind to case-control status. One case and 14 controls were interviewed by telephone.

Ad hoc short-term personal exposure measurements of airborne chlorine and ammonia were performed in a subsample of 10 subjects (four cases and six controls) in the period February-May 2002. One measurement session per individual was performed during domestic cleaning work in one of the homes where the subject was employed. Chlorine and ammonia were measured at the same time with five-seconds intervals using single sensor gas detectors in combination with data loggers (Biosystems, Middletown, CT, USA). The corresponding cleaning tasks and used products were recorded simultaneously. The purpose of this *ad hoc* study was to describe common exposures during domestic cleaning work, and not to compare exposure levels between cases and controls.

Respiratory Symptoms, Lung Function and Allergy Testing

The case-control interview included questions on a variety of respiratory symptoms and chronic conditions, medication use and smoking habits obtained from the ECRHS questionnaire.[112] Subjects performed at least three acceptable reproducible spirometric manoeuvres following standard spirometry procedures.[124] Forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were determined. Predicted values were obtained from Spanish reference equations.[125] Chronic obstructive pulmonary disease (COPD) was defined as both a FEV_1 less than 80% of its predicted value and a FEV_1 to FVC ratio less than 0.7.[126] Methacholine challenge was carried out using a dosimeter (Mefar, Brescia, Italy) according to ECRHS methodology.[127] Bronchial hyperresponsiveness (BHR) was defined as a fall of at least 20% in FEV_1 associated with a methacholine dose of 1 mg (8µmol) or less. Methacholine challenge was not performed for safety

reasons in women with a baseline FEV_1 of either less than 1.5 L or less than 70% of the predicted value. Total and specific serum immunoglobulin (Ig) E levels against ten common environmental aeroallergens (*Dermatophagoides pteronyssinus*, *D farinae*, cat, dog, *Cladosporium herbarum*, Timothy grass, *Parietaria judaica*, *Alternaria alternata* and latex) were determined using the CAP system (Pharmacia Diagnostics, Uppsala, Sweden). Atopy was defined as a specific IgE level of greater than 0.35 kU/L for at least one out of these nine allergens.

Statistical analyses

Considering the large number of cleaning exposure variables, the first analytical step consisted of a quantitative description of all obtained data on products and cleaning tasks. Correlations between continuous frequencies of cleaning tasks and cleaning products were evaluated using Spearman's correlation coefficient (r_s). Associations between case-control status and potential risk factors were estimated by means of the Odds Ratio (OR) with 95% confidence interval (CI) using unconditional logistic regression analysis. Continuous frequencies of cleaning tasks and cleaning products were categorised by default into three exposure groups using tertiles as cut-off points, although variables with a distribution largely skewed to the right were dichotomised using a fixed cut-off point of 12 times per year. Unadjusted ORs for categorised frequencies of all cleaning tasks and cleaning products were calculated. A multivariate model was developed including cleaning tasks and products, current or former employment in non-domestic cleaning jobs, and a history of inhalation accidents related to cleaning products. Exposure variables that showed an unadjusted *P* value less than 0.1 in any of the categories were considered for multivariate modelling. Mutual associations between all exposure variables were evaluated to anticipate potential colinearity and confounding. Explanatory variables with a *P* value less than 0.1 were maintained in the final model. All steps in the multivariate modelling process were adjusted for age tertile and smoking status (never, current and former). The

final multivariate model was obtained for all cases, and subsequently also applied for asthma cases and for chronic bronchitis cases, using all controls as comparison group. All analyses were done using Stata version 7 (Stata Corporation, College Station, Texas, USA).

RESULTS

The mean age of the study population was approximately 50 years, and similar for cases and controls (Table 1). Current smoking was in general uncommon but more prevalent in cases than in controls. At the time of the case-control interview, 14 women reported current asthma symptoms only, 16 reported chronic bronchitis symptoms only and 10 reported both types of symptoms. FEV_1 was very close to the predicted value both for cases and controls, but the prevalence of bronchial hyperresponsiveness was higher in cases than in controls. The prevalence of atopy was the same in cases and controls, although the mean total serum IgE level was higher in cases. Of the 24 cases with asthma symptoms, 16 (67%) reported their first attack of asthma after starting working as a domestic cleaner. Among the 26 chronic bronchitis cases, 14 had chronic cough only, six had chronic phlegm only, and six reported both.

Total duration of employment in domestic cleaning and current number of working hours per week was comparable for cases and controls (Table 1). The median number of homes where women were currently employed was two (range one to seven) in both cases and controls. Present or past employment in a non-domestic cleaning job was reported more frequently by cases than by controls (OR 6.4 (95% CI, 2.9 to 15)), but employment in other jobs with asthma-related exposures was similar (OR 0.7 (0.3 to 1.5)). More than half of the study population reported having at some time accidentally inhaled an important quantity of

vapours, gas or fumes when using cleaning products. This had occurred more frequently in cases compared to controls (OR 3.3 (1.5 to 7.4)). About two thirds of the reported accidents were related to the mixing of two or more cleaning products, principally mixtures with bleach. Accidents related to one single product predominantly involved hydrochloric acid or ammonia.

Most cleaning tasks were performed by the vast majority of the cleaning women, but the frequency of performance varied substantially between tasks (Table 2). Some of the tasks such as cleaning the bathroom or sweeping were performed on average more than once a day, whereas other tasks such as cleaning the oven were normally performed once or twice a month. Most of the tasks were performed with a similar frequency by cases and controls; statistically significant associations were only found for intermediate frequency of mopping the floor (positively) and high frequency of vacuuming (negatively).

Considerable differences were found between the frequency of use of different cleaning products, regarding both the number of users and the frequency of performance (Table 3). Products like detergents or liquid multi-use cleaning products were used by almost all women daily, whereas the use of products like undiluted ammonia and hydrochloric acid was much less common. Statistically significant associations were found for ammonia and degreasing sprays or atomizers, which were more frequently used by cases; and for liquid multi-use cleaning products, which were more frequently used by controls. Similar ORs were found for undiluted and diluted bleach use; and for undiluted and diluted hydrochloric acid.

Correlations between cleaning tasks and cleaning products were in general weak (data not shown). The highest Spearman's correlation coefficients (r_s) between continuous frequencies were observed for obviously dependent combinations such

as 'washing clothes by machine' and 'detergents' (r_s 0.93), or 'cleaning the bathroom' and 'cleaning the toilet bowl' (r_s 0.85). Other correlation coefficients were considerably lower. The only statistically significant negative correlation was between vacuuming and sweeping (r_s –0.20).

When all the relevant exposures were included in a multivariate model the use of bleach, washing dishes and the use of multi-use cleaning products remained as the most influential exposures (Table 4). The use of bleach, either diluted or undiluted, was reported more frequently by cases compared to controls. This resulted in a strong and significant association with a high level of exposure (OR 4.9), as well as an exposure-response trend (X^2 8.0 (P<0.01)). Also, frequency of washing dishes was positively associated (ORs 3.2 and 3.1; X^2 4.4) with symptoms of asthma and chronic bronchitis, whereas using liquid multi-use cleaning products was negatively associated (ORs 0.3 and 0.2; X^2 3.5). Finally, a high risk for asthma and chronic bronchitis symptoms was observed for any history of non-domestic cleaning work. Although confidence intervals were wide due to the limited number of cases, the observed associations with bleach and accidental inhalation were more evident for asthma cases than for chronic bronchitis cases. When the analysis was further restricted to the 14 cases with exclusively asthma, ORs remained very similar as those shown for all 24 asthma cases, with exposure to bleach showing ORs of 23 (95% CI, 1.9 to 274) and 14 (1.3 to 153) for intermediate and high levels, respectively.

Airborne exposure levels of both chlorine and ammonia were detectable (that is, ≥0.1 ppm) during domestic cleaning work in all 10 measurement sessions. In Figure 2 exposure patterns are shown for one of the measurement sessions. In this case elevated chlorine levels were related to the use of bleach for bathroom cleaning, and high ammonia levels were related to the use of ammonia for kitchen cleaning. All 10 women used more than one cleaning product during the

measurement session, particularly for cleaning the bathroom or the kitchen. Nine out of the 10 women used bleach during the measurement session, while the other used two other cleaning products containing chlorine-releasing agents. Chlorine was detected during all sessions; the median levels ranged from 0 to 0.4 ppm and peaks ranged up to 1.3 ppm. Four out of the 10 women used ammonia during the measurement session, while others used cleaning atomizers containing less than 1% of ammonia according to the manufacturers' information. Airborne ammonia was detectable during all sessions; the median levels ranged from 0.6 to 6.4 ppm while peaks ranged up to more than 50 ppm.

DISCUSSION

This nested case-control study is the first epidemiological investigation specifically designed to identify which occupational exposures are related to the risk of asthma and chronic bronchitis symptoms in domestic cleaning workers. The study evaluated exposures to a large range of activities and products, the majority of which were essentially similar for cases and controls. Frequent use of bleach was independently associated with respiratory symptoms, predominantly of asthma. Current or former employment in non-domestic cleaning work and antecedents of an accidental inhalation of large amounts of vapours, gas or fumes from cleaning products were also associated with an increased risk. The findings of our study suggest that the main determinants of increased risk of asthma symptoms among women employed in domestic cleaning are chronic exposures to inhaled irritants.

The use of bleach, which was extremely common in our study population, was consistently associated with respiratory symptoms and particularly with symptoms of asthma. The active component of household bleaches is the chlorine-releasing agent sodium hypochlorite in amounts that are equivalent to 3 to 10%

available chlorine, a strong airway irritant gas.[129] Manufacturers add typically around 1% of sodium hydroxide to bleach as a product stabilizer in order to keep the pH in the alkaline region and hence to inhibit chlorine release.[101] Nevertheless, our exposure measurements showed readily detectable amounts of free chlorine during normal bleach use without mixing with other cleaning agents, including situations where bleach was applied after dilution in water. Washing the dishes more than daily was also associated with asthma and chronic bronchitis symptoms. Although specific information on applied products for dishwashing was not obtained, most likely this referred predominantly to manually doing the dishes using water with dishwashing liquid. Interestingly, mixing bleach with dishwashing liquid was not uncommon in this population, being reported as common practice by 25% of the cases and 15% of the controls. A chemical reaction of hypochlorite from the bleach with either ammonium salts from the dishwashing liquid, or with organic matter from the dishes may lead to the release of chloramines.[130] We also found indications that the use of other irritant cleaning agents such as degreasing sprays or atomizers, hydrochloric acid and ammonia might be related to asthma and chronic bronchitis symptoms, although these exposures did not remain in the final model. The active component of degreasing sprays is sodium hydroxide (up to 5%), a mucous membrane irritant. Although sodium hydroxide is not volatile, the application through spraying may facilitate respiratory exposure to liquid aerosols containing this strong alkaline irritant. Concentrated hydrochloric acid (around 20%) is sold as a cleaning product in Spain, known as *Aguafuerte* or *Salfuman(t)*. Household ammonia is commercially available as a 4 to 10% solution of aqueous ammonia, which is very volatile. Our measurements showed that common household application of ammonia results in relevant airborne exposure levels, with 5-second time-weighted average peaks of more than 35 ppm, the 15-minute average short-term occupational exposure limit in many countries. Thus, the agents associated with respiratory symptoms in our study are of irritant nature and their chronic use in occupational domestic cleaning

may have involved harmful inhalatory exposures likely to result in increased prevalence of asthma and possibly chronic bronchitis.

Within our population of domestic cleaning women, current or former employment in non-domestic cleaning was strongly and independently associated with symptoms of asthma and chronic bronchitis. This finding is consistent with our previous cross-sectional analysis where despite no association between exclusively non-domestic cleaning and respiratory symptoms, those reporting simultaneous employment in domestic and non-domestic cleaning were at an increased risk[120] suggesting the presence of an interaction. In theesence of an interaction. In the cases and controls were domestic cleaners and, consistent with the latter interaction, those reporting non-domestic cleaning activities were also at an increased risk although the mechanism responsible for this interaction remains unclear. In addition, the response rate in the present study was slightly higher in cases reporting non-domestic cleaning thus providing an additional explanation for an increased risk in this group.

We defined case status based on the presence of symptoms of asthma and chronic bronchitis since our population-based survey had shown that employment in domestic cleaning was equally associated with both asthma and chronic bronchitis symptoms.[120] The presence of respiratory symptoms usually shows a large temporal variability[121] and we adopted a restrictive definition of cases and controls as those reporting or denying, respectively, symptoms both at the time of the population-based survey and at the time of the case-control interview. This approach is conservative because the time period elapsed between the two interviews was relatively short (from June 2000 to April 2002), and we assumed that change in symptom status between both interviews may have been importantly biased by measurement error in self-reported symptoms.[131] The validity of our case definition is supported by the large difference in the rates of

BHR (18% versus 3%) and increased total IgE (27% versus 6%) between cases and controls. The observed prevalence of BHR is consistent with data reported in a population-based study of asthma in young adults in Spain with 11% of asymptomatic subjects and 22% of asthmatics showing BHR.[132] FEV_1 levels were, on average, very similar for cases and controls although the number of cases with a reduction in FEV_1 qualifying for COPD was present in 6% of cases and 1% of controls, a difference that was consistent with the higher prevalence of a lifetime smoking history among cases (38%) compared to controls (17%). Atopy was very similar in cases and controls strongly suggesting that increased prevalence of respiratory symptoms in cleaners was not mediated by an allergic mechanism. This is consistent with a previous observation that atopy in cleaning workers with asthma was less common than in office workers with asthma.[118] In addition, we have previously reported that specific sensitisation to allergens potentially related to domestic cleaning activities like detergent enzymes was not observed in cleaning workers.[68] For this reason, we did not test specific sensitisation to detergent enzymes in our study. Although our sample size precludes any strong inference about separating the effects of occupational exposure for asthma and chronic bronchitis, it is of interest that the observed associations with irritants were particularly strong for women with asthma symptoms and much less for those with chronic bronchitis symptoms. The latter is also reassuring that the associations between respiratory symptoms and cleaning exposures were not due to residual confounding by smoking, which is more strongly related to chronic bronchitis than to asthma.

Our study was restricted to prevalent cases and consequently the results referring to work-related symptoms make it impossible to disentangle whether the investigated exposures were responsible for new-onset disease or produced the aggravation of a pre-existing disease.[37] The epidemiological evidence relating occupational exposure to irritants and respiratory symptoms is scarce and is

mostly related to occupational asthma. New-onset asthma has been suggested to result from recurrent or chronic occupational exposures to moderate levels of airway irritants.[46,47,81] The latter has been described after repeated exposures to among others chlorine,[133] ammonia and alkaline agents[81] and to other not specified cleaning agents.[46] Occupational asthma due to chronic exposure to chloramines has been described in a case series of swimming pool workers.[130] The exposures alluded to above are similar to the exposures associated with symptoms in our study, and therefore one plausible explanation is that the type of effects associated to occupational domestic cleaning correspond to those described in the context of so-called "low-dose RADS". In addition, a large number of women in our study reported antecedents of accidental inhalation of high levels of irritants, an exposure that has been associated with the development of RADS; persistent asthma with a sudden onset.[41] The accidents reported in our study were predominantly related to inadequate mixtures of bleach with either hydrochloric acid or ammonia, leading to a rapid release of important amounts of free chlorine and chloramines, respectively.[95,96] Cases of RADS have been related to a variety of respiratory irritants, including chlorine, ammonia and hydrochloric acid.[40,134] Both case reports and surveillance studies show consistent evidence for RADS due to cleaning agents, although the epidemiological and retrospective nature of our study makes it impossible to assess the presence of RADS cases in this workforce-based population. Finally, the association between chronic exposure to irritants and chronic bronchitis may be also a partial explanation for our results since it has been recognised that regular exposure to airway irritants in the workplace may lead to mucus hypersecretion and to chronic productive cough in the absence of asthma, often referred to as chemical or industrial bronchitis.[135,136]

There are a number of limitations in our study that should be considered. First, results were based on self-reported frequencies of current specific cleaning exposures involving the possibility of misclassification. If present, this was

probably non-differential and could have resulted in a bias towards the null. Although the possibility of reporting bias cannot be discarded, the fact that for most reported exposures the frequency was similar in cases and controls was against this possibility. Furthermore, it is not unlikely that the recall of inhalation accidents related to cleaning products and subsequent symptoms was more likely for cases than for controls. This may partly explain the observed positive association for reported accidents. Selection bias might be related to the fact that more cases than controls had abandoned the use of highly irritant cleaning agents for respiratory health reasons, as suggested in our study for undiluted hydrochloric acid (results not given). Consequently, this has probably led to an underestimation of the risks associated with these exposures. Second, due to the restrictive case definition and to a not negligible non-response, despite having identified 117 potential cases, we ended up with 40 in this analysis. This small sample size led to a limited statistical power for the analyses and some potentially relevant associations may have remained undetected. Finally, certain statistical associations observed in our study were not anticipated and are not easy to interpret. The finding of a negative association between symptoms and the use of liquid multi-use cleaning products has no obvious explanation. However, considering the large number of products involved in domestic cleaning, competing exposures for a given task is likely to occur. In other words, if cases are more likely to use bleach or other irritants as a consequence of a true effect they may be less likely to use other competing products, which at their turn will exhibit negative associations with case status. This possibility is supported by correlations between multi-use and ammonia that were negative among cases and positive among controls (results not given).

The findings reported in the present study may have significant implications for public health. Domestic cleaning is in many countries one of the largest occupational categories among women, implying relevant attributable risks for

respiratory disease. As far as we know this is the first study reporting respiratory morbidity in women employed in domestic cleaning. Several factors may have contributed to the lack of studies in this workforce, mainly a tendency to neglect occupational health problems in women and the usual unregulated nature of this type of work. Although we focused on respiratory morbidity, other health problems like musculoskeletal morbidity, dermatitis or psychosocial disorders may also be relevant in this population.[137] Cleaning products are also used in a large number of other occupational settings. Results from a recent surveillance study in the United States demonstrated that 78% of work-related asthma cases due to cleaning products occur in non-cleaning occupations such as nurses or clerical workers.[86] In addition, a large proportion of the general population is potentially at risk when cleaning their own home. Another United States surveillance study showed that exposure to household cleaning agents was among the most frequent causes of non-work-related hospital admission for chemical-related respiratory disease.[87] The use of bleach, which was found to be associated with respiratory symptoms, is widespread in Spanish homes as a conventional cleaning product. Unpublished results of the follow-up of the ECRHS[122] showed that the use of household bleach varied widely across European countries. Although its use was most common in Spain, in several other European countries more than half of the homemakers reported using bleach at least once a week. Respiratory health effects of non-professional home cleaning exposures require further study.

In conclusion, asthma symptoms in domestic cleaning women are related to the regular use of bleach and possibly other irritant products, pointing towards an irritant-induced effect mechanism. Further research is needed to investigate the public health impact of the use of irritant cleaning products in cleaning workers, in other occupations and in the household.

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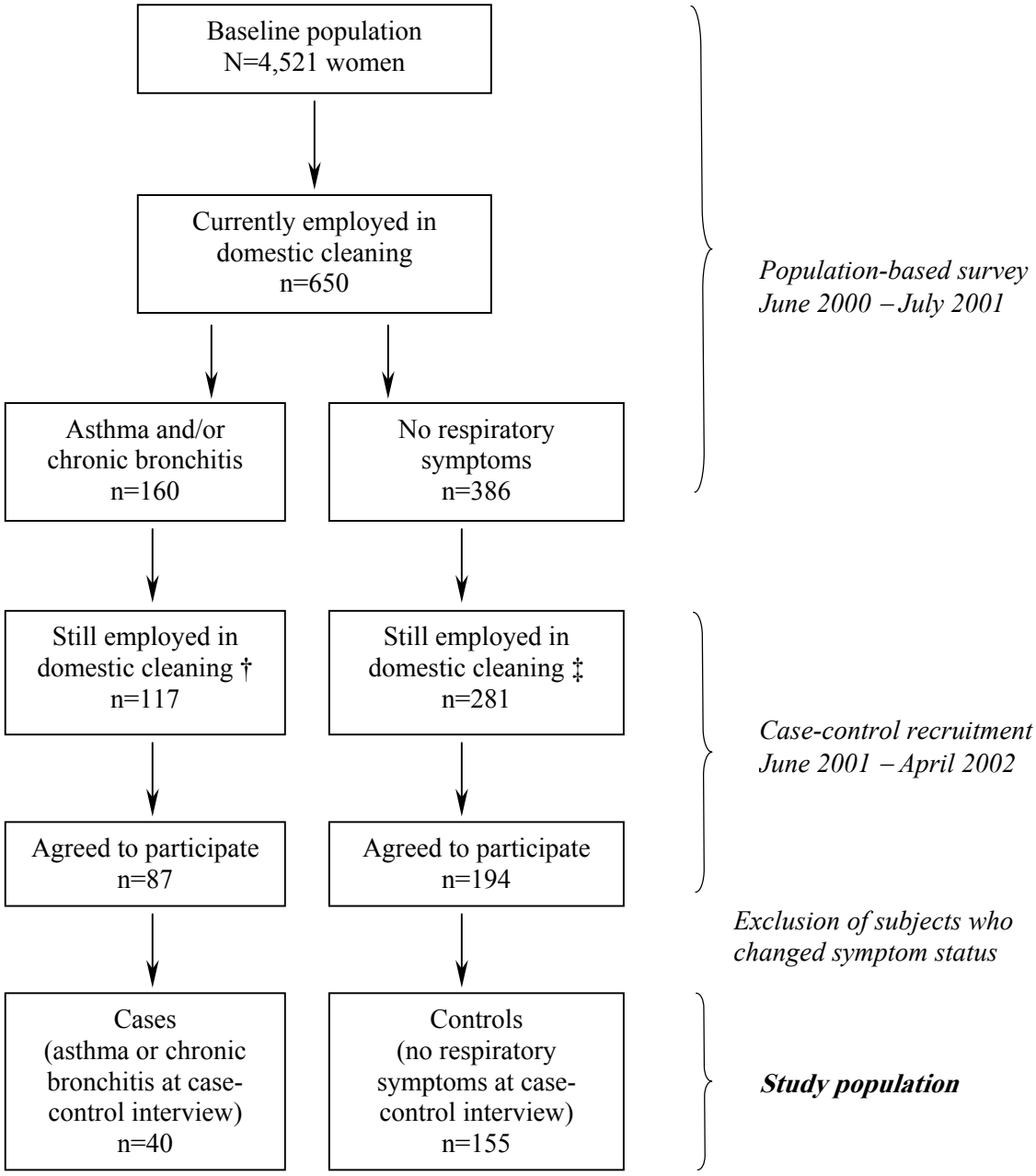
ETHICS APPROVAL

The study protocol was approved by the Clinical Research Ethical Committee of the Municipal Institute of Health Care (CEIC-IMAS), created and accredited on November 11, 1993 by the General Management of Health Resources of the Generalitat de Catalunya, in accordance with an 'Ordinance dated October 26, 1992'.

Figure 1. Selection of the population for a case-control study among women employed in domestic cleaning, nested within a population-based survey*



* See reference 120. † 38 women with symptoms had quit domestic cleaning employment and five had moved from the study area during the period elapsed between the population-based survey and the case-control recruitment. ‡ 97 women without symptoms had quit domestic cleaning employment and eight had moved from the study area during the period elapsed between the population-based survey and the case-control recruitment.

Table 1. Demographic, respiratory health and occupational characteristics of the study population

	Cases		Controls	
Total number	40	(100%)	155	(100%)
Age (years)	48	(31 to 64)	51	(33 to 65)
Current smokers	11	(28%)	15	(10%)
Ex-smokers	4	(10%)	10	(7%)
Asthma symptoms *	24	(60%)	0	(–)
Chronic bronchitis symptoms †	26	(65%)	0	(–)
FEV_1 (% of predicted) ‡	99	(68 to 127)	99	(72 to 125)
COPD § ‡	2	(6%)	1	(1%)
Bronchial hyperresponsiveness ||	4	(18%)	3	(3%)
Atopy ¶ **	6	(16%)	19	(15%)
Total serum IgE >100 kU/L **	10	(27%)	8	(6%)
Current working hours per week in domestic cleaning	18	(3 to 50)	16	(3 to 80)
Years of employment in domestic cleaning	16	(2 to 53)	17	(1 to 53)
Ever employed in a non-domestic cleaning job	31	(78%)	54	(35%)
Ever employed in a non-cleaning job with asthma-related exposures ††	11	(28%)	55	(35%)
Ever inhaled an important quantity of vapours, gas or fumes related to cleaning agents	31	(78%)	79	(51%)

Number (%) or median (minimum to maximum) are given. * Asthma attack and/or nocturnal attack of shortness of breath in the last 12 months. † Regular cough and/or regularly bringing up phlegm. ‡ N=35 cases and 126 controls. § FEV_1<80% of predicted and FEV_1 to FVC ratio <70%. || Fall of at least 20% in FEV_1 associated with a methacholine dose of ≤1mg; n=22 cases and 95 controls. ¶ Specific serum IgE to at least one out of 10 common allergens. ** N=37 cases and 126 controls. †† Assessed by using a job exposure matrix with additional expert judgement.[123]

Table 2. Associations (unadjusted Odds Ratios and 95% Confidence Intervals) between asthma / chronic bronchitis symptoms, and the frequency of performance of cleaning tasks

Cleaning task	Current performance (N=195)		OR (95% CI) associated with exposure level †	
	Subjects (%)	Median freq.* (times/year)	Intermediate	High
General				
Dusting	100	364	1.2 (0.5 to 2.7)	1.2 (0.5 to 2.8)
Mopping the floor	99	364	2.8 (1.2 to 6.8)	1.1 (0.4 to 3.1)
Cleaning windows or mirrors	99	260	1.6 (0.7 to 4.0)	1.9 (0.8 to 4.7)
Sweeping	92	416	1.1 (0.5 to 2.4)	0.9 (0.4 to 2.2)
Vacuuming	91	180	0.6 (0.3 to 1.4)	0.4 (0.2 to 1.0)
Carpet or rug beating	35	52		1.0 (0.5 to 2.2)
Kitchen cleaning				
Superficial kitchen cleaning	100	468	0.6 (0.3 to 1.4)	0.6 (0.2 to 1.4)
Cleaning the stove or the hob	99	520	1.1 (0.5 to 2.7)	0.5 (0.2 to 1.2)
Thorough kitchen cleaning	99	24	2.2 (1.0 to 5.3)	1.1 (0.4 to 2.9)
Thorough cleaning of the fridge	99	14	0.9 (0.4 to 2.2)	1.2 (0.5 to 2.8)
Washing dishes	97	416	2.0 (0.8 to 5.1)	2.3 (1.0 to 5.3)
Cleaning the microwave	89	134	1.3 (0.5 to 3.0)	0.9 (0.4 to 2.1)
Cleaning the oven	85	24	2.0 (0.8 to 5.0)	1.9 (0.8 to 4.7)
Bathroom cleaning				
Cleaning the bathroom	100	468	1.1 (0.4 to 2.6)	1.1 (0.5 to 2.5)
Cleaning the toilet bowl	99	520	0.6 (0.2 to 1.4)	1.1 (0.5 to 2.5)
Laundry				
Washing clothes by machine	100	364	1.1 (0.5 to 2.6)	0.6 (0.3 to 1.5)
Ironing	99	208	0.5 (0.2 to 1.2)	0.7 (0.3 to 1.6)
Washing clothes by hand	63	104		0.9 (0.4 to 1.7)

* Median frequency among women reporting current performance of cleaning task. † N=40 cases and 155 controls. Exposure levels in either two (fixed cut-off level of 12 times/year) or three (tertiles) categories; low exposure level was used as reference category.

Table 3. Associations (unadjusted Odds Ratios and 95% Confidence Intervals) between asthma / chronic bronchitis symptoms, and the frequency of use of cleaning products

Cleaning product	Current use (N=195)		OR (95% CI) associated with exposure level †	
	Subjects (%)	Median freq.* (times/year)	Intermediate	High
Irritant products; used undiluted ‡				
Bleach	82	260	1.9 (0.7 to 5.0)	2.4 (1.0 to 6.1)
Ammonia	16	14		3.1 (1.2 to 8.0)
Hydrochloric acid	30	6		2.2 (0.9 to 5.3)
Irritant products; used diluted §				
Bleach	90	312	1.6 (0.7 to 4.0)	2.3 (0.9 to 5.4)
Ammonia	56	52		0.8 (0.4 to 1.7)
Hydrochloric acid	11	12		1.6 (0.5 to 5.5)
Sprays or atomizers				
For glass cleaning	90	232	0.6 (0.2 to 1.5)	1.7 (0.7 to 3.7)
For degreasing	84	103	1.3 (0.5 to 3.3)	2.6 (1.1 to 6.0)
For furniture cleaning	72	116	1.6 (0.7 to 3.9)	1.7 (0.7 to 4.0)
For floor mopping	47	104		0.7 (0.3 to 1.4)
Insecticides	42	34		1.3 (0.6 to 2.8)
For oven cleaning	39	20		1.2 (0.5 to 2.5)
For air refreshing	30	84		1.6 (0.8 to 3.4)
For ironing	27	52		0.6 (0.3 to 1.5)
For cleaning carpets, rugs or curtains	15	6		2.0 (0.6 to 7.0)
Other products				
Detergents	100	364	1.4 (0.6 to 3.0)	0.6 (0.2 to 1.5)
Liquid multi-use cleaning products	95	364	0.6 (0.3 to 1.3)	0.4 (0.2 to 1.0)
Decalcifiers	70	52	0.9 (0.4 to 2.1)	1.2 (0.5 to 2.7)
Stain removers	35	52		0.9 (0.4 to 2.0)
Polishes, waxes	34	52		0.9 (0.4 to 2.0)
Drain-cleansing agents	23	3		0.0 (–)
Dry-cleaning foams	19	4		2.0 (0.6 to 7.0)

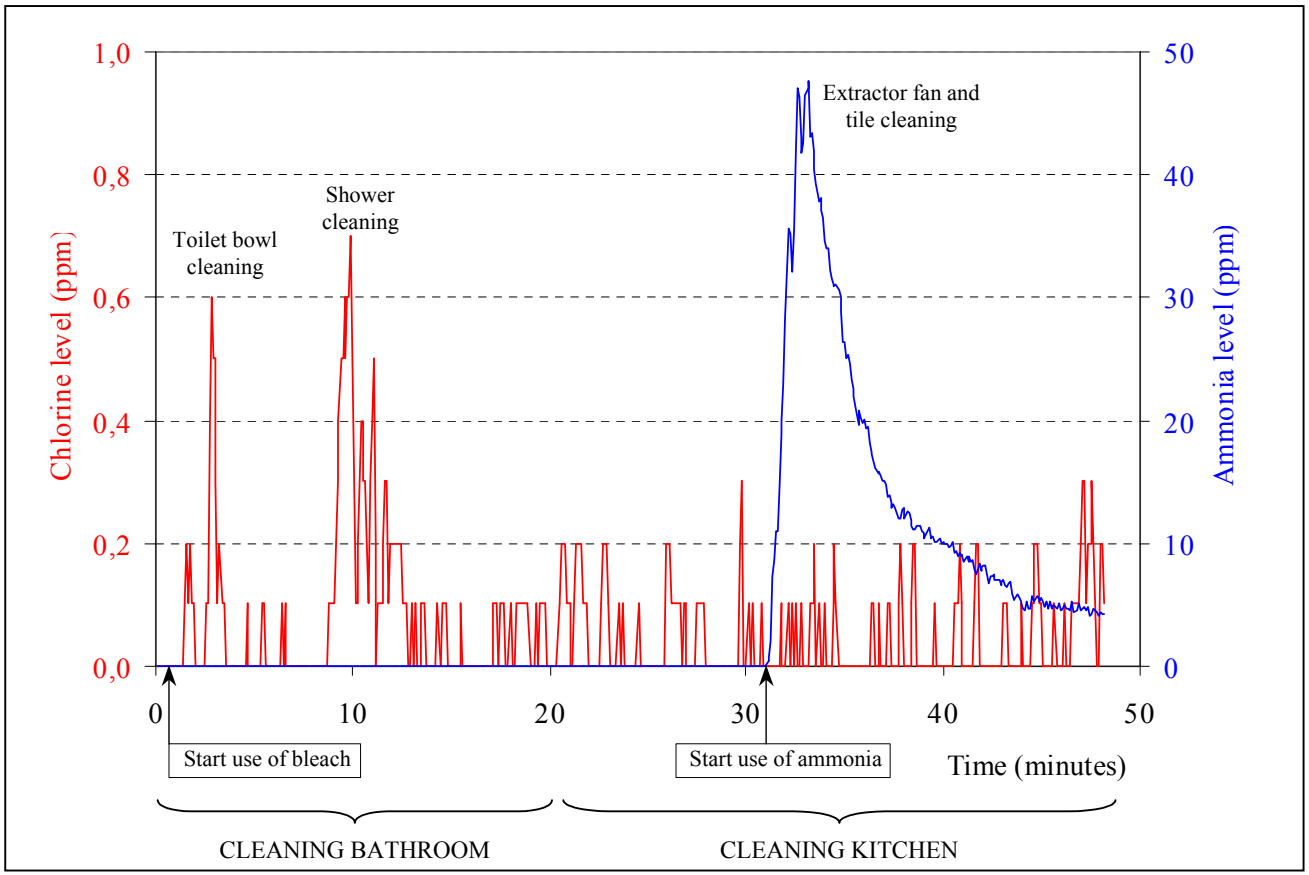
* Median frequency among women reporting current use of cleaning product. † N=40 cases and 155 controls. Exposure levels in either two (fixed cut-off level of 12 times/year) or three (tertiles) categories; low exposure level was used as reference category. ‡ Product used directly as commercially available. § Product diluted in a bucket of water before being used.

Table 4. Multivariate associations (adjusted Odds Ratios and 95% Confidence Intervals) between asthma / chronic bronchitis symptoms, and risk factors

	Controls (n=152*)	All cases (n=40)	OR (95% CI)	Asthma (n=24)	OR (95% CI)	Chronic bronchitis, no asthma (n=16)	OR (95% CI)
Bleach (both undiluted and diluted)							
<364 times/year	56	8	1.0	3	1.0	5	1.0
364 to 640 times/year	53	11	3.3 (0.9–11)	9	10 (1.7–60)	2	0.9 (0.1–6.5)
≥640 times/year	43	21	4.9 (1.5–15)	12	12 (2.3–67)	9	2.6 (0.6–12)
Use of liquid multi-use cleaning products							
<266 times/year	50	20	1.0	13	1.0	7	1.0
266 to 480 times/year	51	12	0.3 (0.1–0.8)	6	0.2 (0.0–0.7)	6	0.3 (0.1–1.6)
≥480 times/year	51	8	0.2 (0.1–0.6)	5	0.1 (0.0–0.5)	3	0.2 (0.0–1.3)
Washing dishes							
<376 times/year	64	10	1.0	8	1.0	2	1.0
376 to 520 times/year	37	12	3.2 (1.0–10)	6	2.0 (0.5–8.9)	6	7.5 (1.0–53)
≥520 times/year	51	18	3.1 (1.1–8.9)	10	3.8 (1.0–14)	8	6.5 (0.9–47)
Inhalation of an important quantity of vapours, gas or fumes related to cleaning agents							
Never	73	9	1.0	5	1.0	4	1.0
Ever	79	31	2.3 (0.9–6.1)	19	3.8 (1.0–14)	12	0.9 (0.2–4.3)
Employment in non-domestic cleaning							
Never	101	9	1.0	5	1.0	4	1.0
Ever	51	31	8.5 (3.2–23)	19	12 (3.2–46)	12	7.9 (1.6–39)
Smoking							
Never	127	25	1.0	19	1.0	6	1.0
Currently	15	11	4.1 (1.1–15)	2	0.5 (0.1–3.9)	9	22 (3.6–137)
Formerly	10	4	5.3 (1.1–25)	3	5.5 (0.9–33)	1	8.9 (0.5–173)

Multiple logistic regression analyses adjusted for all listed variables and age tertile. * Three controls had missing values for one or more of the exposure variables and were not included in this multivariate model.

Figure 2. Pattern of personal airborne chlorine and ammonia exposure (5-second time-weighted average) during domestic cleaning work



The graph corresponds to a 55-year old woman with a history of 26 years in domestic cleaning work, currently employed in one home for cleaning eight hours weekly. Chlorine and ammonia concentrations in ppm are indicated by the red and the blue line, respectively. Recommended occupational exposure limits (15-minute time-weighted average) amount to 0.5 ppm and 35 ppm for chlorine and ammonia, respectively.[128]

6. PAPER # 3

Short-Term Effects of Cleaning Exposures on Respiratory Symptoms and Peak Expiratory Flow in Women Employed in Domestic Cleaning: a Panel Study*

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* M M-Ramon, Zock JP, Kogevinas M, Sunyer J, Basagana X, Schwartz J, Burge PS, Huggins V, Anto JM. Short-term respiratory effects of cleaning exposures in domestic cleaning women. **European Respiratory Journal** 2006 Mar 1; [Epub ahead of print].

7. GENERAL DISCUSSION

The objective of this section is to globally discuss the findings of the EPIASLI study by examining how the three parts here presented interrelate and contribute to answer the questions arisen in the objectives section. The aim here is not to repeat the content of the papers, but to discuss thoroughly several aspects already mentioned and to offer a broader overview of the problem.

7.1. Interpretation of the Main Findings

Cleaning work is an occupation that has recently been recognized to be at risk for work-related asthma. In the course of the EPIASLI study, a number of scientific papers have evidenced the relevance of work-related asthma in cleaning workers,[50,51,58,59,63,64] as well as the involvement of cleaning agents in asthma cases occurring in other occupations (including homemakers).[63,64,86] Our study focused on domestic cleaning women, a large workforce where occupational health has been largely neglected. When the EPIASLI study started, the only evidence of an increased asthma risk in this sector came from results in a small sample of the ECRHS.[68] In such a context, we followed a logical sequence in epidemiology: first confirm these results and then look into the possible related exposures. Initially, we conducted a population-based survey aiming to confirm the increased risk of asthma symptoms in domestic cleaners and to evaluate also other respiratory disorders potentially associated with this occupation. Results from the population-based survey, not only confirmed the excess risk of asthma symptoms in domestic cleaners, but also showed an increase in the risk of chronic bronchitis symptoms

independently of asthma. Therefore, the subsequent nested case-control study and panel study among domestic cleaners included cases with asthma and/or chronic bronchitis symptoms. Due to the limited knowledge about the specific cleaning exposures related to respiratory symptoms in cleaning workers, we examined a wide range of exposures. These two studies allowed us to investigate the effects of both chronic and transient exposure to specific cleaning agents/activities on the respiratory health of domestic cleaning women.

■ *Respiratory Health in Domestic and Non-Domestic Cleaning Women*

Results from the population-based survey showed increased risks of asthma and chronic bronchitis symptoms in domestic cleaning women as compared with women that had never worked in cleaning. Although there is some evidence in the literature that non-domestic cleaning workers also have an increased risk of asthma,[48,50] this was not apparent in our study. Nevertheless, the group of non-domestic cleaners was very heterogeneous and analyses within the group of current non-domestic cleaners suggested increased risks in hospital cleaners and possibly other subgroups.

Although asthma risks may vary between different types of cleaning workers, the increased risks observed in several studies among cleaners employed in different settings[50,48,68] suggest the existence of common occupational risk factors inherent to cleaning work. In spite of this, differences in the exposure pattern can be expected for cleaners employed in different sectors and may be related to the observed differences in risk. It is noteworthy that cleaning exposures related to an increased risk of respiratory symptoms in the case-control and in the panel study, such as washing dishes or using degreasing sprays/atomizers, are characteristic of domestic cleaning work and probably less common in other cleaning jobs. This

could partially account for the higher risks of asthma and chronic bronchitis symptoms observed among domestic cleaners in our study.

Paradoxically, despite the lack of association between current non-domestic cleaning and respiratory symptoms in our study, those reporting simultaneous employment in domestic and non-domestic cleaning had higher risks than those exclusively employed in domestic cleaning. Although there is no easy explanation for this interaction, a longer duration of daily or weekly exposure to cleaning work could account for the increase of risk in those employed simultaneously in domestic and non-domestic cleaning. This is supported by results in the panel study where aggravation of lower respiratory symptoms was observed on days with longer duration of exposure. Thus, although this is highly speculative, it can be hypothesized that obstructive lung disease in domestic cleaning women is aggravated by employment in non-domestic cleaning due to a more recurrent exposure to cleaning agents.

■ *Respiratory Health in Current and Former Cleaning Women*

The population-based nature of the first cross-sectional survey allowed us to estimate the prevalence of respiratory symptoms not only in current cleaners, but also in women that used to work as cleaners in the past. Some individuals tend to quit their job when they become ill, leading to an increase in the prevalence of illness among former workers and improving the health status of the workforce.[153] Consistent with this survivor effect,[34] we found higher risks in former than in current cleaning workers. However, leaving the job for respiratory health reasons was reported by a small proportion of former cleaners, accounting only partially for the observed differences in risk.

The exposure pattern of cleaning workers has probably changed over the years, providing an additional explanation for differences in risks between current and former cleaners. Although during the last decades the amount and variety of cleaning products has remarkably increased, in the past the choice was limited to few traditional cleaning products. This included bleach, invented by Labarraque in the 19th century[154] and widely used in Spanish homes.[101] A more frequent use of this disinfectant by former domestic cleaners could have contributed to the increased risk of asthma and chronic bronchitis symptoms in this collective. In addition, as claimed by manufacturers, cleaning products are continuously improved to be safer for human health[155] and to provide the same results with less effort, less time (of exposure) and less quantity of product. Finally, technological innovations such as dishwashers, washing machines or vacuum cleaners are also likely to have introduced differences in the exposure pattern of domestic cleaning workers over time.

■ *The Exposure Pattern of Current Domestic Cleaning Women*

Being the first epidemiological study to thoroughly investigate occupational exposures in domestic cleaners, the EPIASLI study offered a valuable insight into the complex exposure pattern of this workforce. This complexity is closely related to the informal nature of this occupation, which results in a relatively high intermittence of employment and frequent changes of employer, as well as irregular working hours and irregular working days. In addition, domestic cleaners work in different occupational settings within the same period of time, being typically employed in more than one home and, in occasions, having also a non-domestic cleaning job. On top of this, they also encounter domestic cleaning exposures during leisure days (if they clean their own home).

The case-control and the panel study showed that domestic cleaners are practically daily exposed to a wide range of cleaning agents, with a longer and more diverse exposure on working days. The frequency of exposure varied considerably across the different tasks/products, being among the most frequent cleaning the stove/hob, cleaning the toilet bowl, washing dishes and using bleach. The frequency distribution for each specific exposure was relatively wide, indicating the existence of inter-individual differences in exposure. This was probably due not only to differences in the number of weekly working hours, but also to different cleaning practices, inevitable in an occupation where no previous training is required.

Personal exposure measurements of airborne substances released from cleaning products were only performed for chlorine and ammonia. Both agents were detectable during regular domestic cleaning work, especially when using bleach and ammonia. Short-term average exposure levels did not exceed the recommended occupational exposure limits. On the other hand, it is noteworthy that accidental exposure to large amounts of vapours, gas or fumes while using cleaning products was remarkably common in the study population, even among controls. Consistently with data from poison control centres[90,91] and surveillance systems,[86] most of the cleaning inhalation accidents in our study involved mixtures with bleach, although single use of ammonia or hydrochloric acid was also frequently reported.

■ *Cleaning Exposures Associated with an Increased Risk of Asthma and/or Chronic Bronchitis Symptoms*

Asthma and chronic bronchitis symptoms in domestic cleaning women were found to be related to several cleaning exposures. Bleach was one of the most important

related exposures, apart from being the most frequently used cleaning product. The adverse effect of bleach was evident both in the case-control and in the panel study. Regular exposure to bleach (more than once a day) was associated with symptoms of obstructive lung disease, and transient exposure to bleach was related to the aggravation of symptoms in those with respiratory disorders. Consistently, bleach was reported as the most common causative agent among work-related asthma cases due to cleaning agents in a surveillance programme in the United States.[86]

Washing dishes more than once a day was also associated with an increased risk of asthma and/or chronic bronchitis symptoms in the case-control study. Although the specific product used to perform this task was unknown, it can be assumed that it was predominantly dishwashing liquid. However, it is noteworthy that, when asked in an open-end question about habitual cleaning mixtures used, 25% of cases and 15%of controls reported mixing dishwashing liquid with bleach. This mixture may result in the release of moderate amounts of chloramines, which have been reported as a causative agent for occupational asthma in swimming-pool workers.[130]

Results from the case-control and the panel study suggested also an adverse respiratory effect of exposure to degreasing sprays/atomizers. Although less frequent than using bleach or washing dishes, the use of degreasing sprays/atomizers was not uncommon in the study population (approximately twice a week). The active component of degreasing sprays/atomizers is sodium hydroxide, a mucous membrane irritant that has only occasionally been related to respiratory adverse effects,[82,156] probably due to its non-volatility. Nevertheless, application of degreasers during domestic cleaning work using a spray or an atomizer may facilitate the inhalation of sodium hydroxide.

We found indications that other less frequently used irritant cleaning products, such as ammonia or hydrochloric acid, might also be related to obstructive lung disease in domestic cleaners. Consistently, exposure to ammonia has been reported as a common cause of work-related asthma in the United States[85,86] and hydrochloric acid has been reported to cause asthma in a case-series study.[79] In addition, these two cleaning products are commonly involved in the occurrence of inhalation accidents during cleaning work, which was also an important risk factor for obstructive lung disease in domestic cleaning women.

Finally, using air-refreshing sprays/atomizers was also an important risk factor for aggravation of lower respiratory symptoms in those with respiratory disorders. Results in the case-control study suggested a possible increase in the risk associated to this exposure, but the estimate was not statistically significant. Exacerbations of asthma can occur after exposure to odours such as those present in perfumed cleaning products and air-refreshing sprays/atomizers.[144,145] In addition, some of the compounds used to confer scent to cleaning products, such as pinene[103] or limonene,[104] have sensitising properties.

■ *Asthma and Chronic Bronchitis*

There is considerable clinical overlap between asthma and chronic bronchitis.[135] Distinction between both entities is not straightforward, especially in epidemiological studies where an individual physician's diagnostic is often unfeasible. Most epidemiological studies have used validated symptom questionnaires to define asthma[157] and chronic bronchitis[158] given their simplicity and their convenience in terms of cost, logistics and comparability between populations.[159] In an attempt to reduce the subjectivity of the asthma definition, some studies have used bronchial hyperresponsiveness (BHR) as a marker of

disease, either alone or in combination with symptom questions. It has been recently suggested that a more valid definition of asthma can be obtained using symptom questions alone (without BHR) when the main focus is to estimate differences in asthma prevalence between similar populations.[160]

In our study, we used questions on symptoms to define asthma and chronic bronchitis and additionally measured several clinical features in the subsample of domestic cleaners participating in the case-control study, including BHR, lung function and atopy. The prevalence of BHR was 18% among cases (23% among asthmatics) and 3% among controls. These results were similar to those found in other population-based studies,[132] where, in contrast to the clinical setting, the study population includes many mild or borderline asthmatics.[159] On average, FEV_1 and atopy were very similar for cases and controls. However, consistent with the inclusion of chronic bronchitis cases, there were more cases than controls with a reduction in FEV_1 qualifying for COPD and lifetime smoking history was more common among cases.

Asthma and chronic bronchitis not only share clinical features, but they also show overlap in their pathogenesis.[135] Consistently, in the population-based survey, domestic cleaning work was a risk factor for asthma symptoms as well as for chronic bronchitis symptoms. In agreement with these findings, a case-case study examining the clinical features of asthma in cleaning workers, found that asthma in cleaners was accompanied by symptoms of chronic bronchitis more frequently than in office workers.[118] Therefore, in our case-control study, we defined case status based on the presence of either asthma or chronic bronchitis symptoms. Although the effect of irritant cleaning exposures was more evident for asthma than for chronic bronchitis symptoms, the distinction between these two entities was somewhat difficult due to the small sample size.

■ *Work-Relatedness of Asthma and Chronic Bronchitis Symptoms*

The criteria used in the epidemiological approach to determine the work-relatedness of a disease differ from those used in the clinical setting, where the individual (instead of groups of individuals) is the main focus. Occupational population-based studies typically identify occupationally exposed groups and test whether they have a higher prevalence or incidence of disease than a non-exposed reference group. The excess of subjects affected by the disease in the exposed group is then attributed to work, but identification of the individuals with work-related disease (as ascertained by clinical diagnosis) is rarely performed.[161,162]

In our study, the excess of asthma and chronic bronchitis symptoms in domestic cleaners could be attributed to either onset of new cases induced by occupational exposures or work-aggravation of a pre-existing disease, both equally relevant in terms of prevention.[29] It is also possible that women entering the domestic cleaning workforce had worse respiratory health than those in formal occupations, where little flexibility in working hours is available. However, the fact that those employed simultaneously in domestic and non-domestic cleaning presented the highest risks argue against this possibility, given that non-domestic cleaning is likely to be a formal job.

Assuming that the excess of respiratory morbidity in domestic cleaning workers is due to the presence of work-related cases, there must be (an) occupational exposure(s) responsible for the induction or aggravation of the disease. In the case-control study we identified several cleaning exposures that could potentially be a causal agent such, as using bleach or washing dishes. To further assess the short-term effects of cleaning exposures on the respiratory tract, we used a diary of symptoms and PEF. At the group level, we observed worsening of lower

respiratory symptoms on working days, and specifically on days with exposure to some of the cleaning agents previously identified in the case-control study. This supports the hypothesis that some of the cases among domestic cleaning workers, either induced or not by an occupational exposure, were work-aggravated.

Peak flow diaries are often employed by clinicians as a diagnostic aid to individually assess whether asthma in their patients is work-related.[163] In the panel study we also used this approach to identify which cases could potentially be work-related as ascertained by the Oasys programme[142] and a PEF expert (Burge PS). In this analysis, 30% of the evaluated cases were positively scored for work-related asthma by at least one of the measures. This figure is in close agreement with the expected number of asthma cases (29%) attributable to work among current domestic cleaning workers according to the excess risk observed in the population-based survey.[164]

■ *Induction and Aggravation Mechanisms*

Results from our study showed that domestic cleaning women with respiratory symptoms were more frequently exposed to irritant cleaning products than those without symptoms. Although there is some evidence that occupational exposure to irritant agents can induce chronic bronchitis,[135,136] most of the literature about irritant-induced respiratory diseases relates to occupational asthma. The most accepted type of irritant-induced asthma is the so-called Reactive Airways Dysfunction Syndrome (RADS), which develops shortly after one or more massive exposure/s to respiratory irritants.[40,41,42] In our study, this type of exposure occurred mainly when mixing bleach with other cleaning products or when using ammonia or hydrochloric acid alone. Although some controversies exist,[165] several authors have suggested that frequent low-level exposure to irritants can also

induce new-onset asthma, the so-called low-dose RADS[46] or not-so-sudden irritant-induced asthma.[47] Frequent use of irritant cleaning products like bleach or degreasing sprays, or the habitual mixture of bleach with dishwashing liquid can result in this type of exposure. Therefore, both RADS and low-dose RADS could potentially be responsible for new-onset asthma cases in our population. Unfortunately, due to the epidemiological and retrospective nature of the information here available, distinction between RADS and not-so-sudden RADS is not possible.

Some of the cases in our study may have been induced by occupational exposures and some others may not, but in both situations the disease is liable to be aggravated by work exposures. Exacerbations of asthma[150] and chronic bronchitis[151,152] can occur after inhalation of irritant substances, being particularly susceptible those individuals with irritant-induced asthma.[40] Results from the panel study showed that increase of lower respiratory symptoms and decrements in PEF occurred after exposure to irritant cleaning products such as bleach or degreasing sprays/atomizers, suggesting the existence of an irritant aggravation mechanism.

Although the involvement of an immunological mechanism in the induction or aggravation of obstructive lung disease in domestic cleaning workers cannot be completely ruled out, our findings suggest that this is not the predominant mechanism. This is supported not only by the irritant nature of the cleaning exposures related to the disease, but also by the fact that atopic status was not a relevant risk factor for obstructive lung disease in this workforce. However, this might not be the case for other types of cleaning workers, since results from surveillance programmes in France[59] and the United Kingdom[166] reported sensitisation to mites and latex as important causes of occupational asthma in cleaning workers. In the United Kingdom, sensitisation to latex was especially

relevant in cleaners working in health services. In contrast, in our study none of the participants showed specific IgE against latex.

■ *Domestic Cleaning Work, a Female Precarious Occupation*

The common use of terms like "cleaning lady" or "*mujer de la limpieza*" (in Spanish) evidences the predominance of women in cleaning jobs, and especially in domestic cleaning work, where the proportion of men is known to be insignificant.[68,167,168] These circumstances led us to focus on female workers, thus precluding the recognition of gender differences in the risk associated with cleaning work and its specific occupational exposures. There is some evidence that women's airways are more sensitive to tobacco smoke, and possibly to other irritants, than men's[169] and that the prevalence of BHR in the adult general population is higher among women.[8] Although generalization of our results should be done cautiously, a lower susceptibility to irritants in male workers (if any) could result in lower risks associated to irritant cleaning products. Nevertheless, results from a case-case study within the ECRHS cohort found similar risks associated to cleaning work in men and women.[118] Gender differences in the prevalence of asthma in the adult general population (with a higher prevalence among women) are the result of the complex interaction between environmental and socio-cultural factors with biological host factors.[169] Among the environmental and socio-cultural factors, it could be relevant to include a higher exposure to domestic cleaning activities among women.

For women with a low educational level, domestic cleaning work is one of the few employment options available. This low-salaried precarious occupation is an informal job with a low social and legal protection in many countries. When working without a contract (which in Spain is the usual situation), domestic

cleaners lack benefits such as sick leave or paid holidays and are unprotected against unfair dismissal, extremely low salaries or excessive working hours. In our study, participants worked between 3 and 80 hours per week and most of them reported periods of unemployment. However, it is not unlikely that some of them voluntarily decided to stop working on periods when their "housewife obligations" were too demanding (e.g., when having young children), given the Spanish deep-rooted belief that women are responsible for domestic chores.[170] This situation can influence the self-perception of job insecurity of women whose salary is regarded as a secondary income for the household.

Although our research focused on the effects of domestic cleaning work on respiratory health, due to their precarious working conditions and their low socio-economic status, this workforce is likely to also suffer other health problems. The adverse health effects of having a precarious and/or informal job have been well documented and include psychological disorders,[171,172,173] such as anxiety or depression, as well as physical problems,[174] such as fatigue, backache or muscular pains. Cooper *et al*.[167] found that a substantial proportion of female domestic cleaners reported limitation of activity and a large number of days with restricted activity due to chronic conditions. Another study among Brazilian housemaids showed a high risk of psychological disorders in this workforce[175] and suggested as a possible contributing cause the mental suffering caused by social stigmatisation and discrimination. Other relevant health problems in cleaning workers include skin symptoms[176,177,178] and musculoskeletal morbidity.[179,180] Finally, precariousness of employment is closely related with a low socio-economic status, which has also been associated with worse health status,[181,182] including a higher prevalence of asthma[183] and chronic bronchitis.[184,185]

7.2. Implications

Findings in the EPIASLI study may have significant implications for public health. Cleaning constitutes a large occupational sector in many countries, especially among women, and recent surveillance programmes have evidenced the important contribution of this workforce to the total burden of occupational asthma.[58,63,64] The proportion of cleaning workers employed in private homes is unknown and may vary between countries, but estimates from the ECRHS indicate that it represents approximately one third of all female cleaners in Spain,[68] which in turn represent between six and ten percent of all female workers. In addition, cleaning products have been reported to be responsible for a substantial proportion of work-related asthma cases in other occupations, such as nurses or clerical workers.[86]

Our findings might also have implications for housewives and other people cleaning their own home. Although the frequency of exposure is expected to be lower in the general population, the type of exposures encountered should be essentially the same as in domestic cleaning workers. Data from hospital records and poison control centres have demonstrated that the occurrence of inhalation accidents involving household cleaners is not uncommon in the general population.[87,91] Our findings may be of special interest in Spain, where the use of bleach is particularly frequent. Data of the annual bleach consumption for household applications showed that Spain had the highest consumption per capita (12 litres) of the 13 countries examined.[101] Similarly, unpublished results from the ECRHS showed that use of bleach was most common in Spain (used at least once a week by 80% of the participants), but it was also frequently used in other countries like Italy, France, United Kingdom or Belgium. This suggests that chronic low-level exposure to bleach is likely to occur also in the general population, both in Spain and in other countries.

To our knowledge, the EPIASLI study is the first epidemiological investigation specifically designed to assess asthma risk in domestic cleaning women and its relationship with specific exposures. Findings in our study indicate that respiratory symptoms in domestic cleaning women are related to frequent low-level exposure to several irritant cleaning agents as well as to inhalation accidents. These two types of exposure are believed to be also common in other occupations and in the general population, especially among women.[63,101] Therefore, the population attributable risks for respiratory disease are likely to be of relevance.

7.3. Limitations

In the three scientific papers here presented, there is a comprehensive discussion of the possible limitations of each study. In this section some of the most important weaknesses of the EPIASLI study are thoroughly discussed from a more general and integrative perspective.

In the first place, the self-reported nature of the exposure assessment could have introduced an exposure misclassification[37] in both the population-based survey and the case-control study. In the first instance, some domestic cleaning workers could have withheld their occupation because of its informal nature and/or its lack of prestige. If present, this misclassification was most likely non-differential and would have biased our results towards the null.[186] In the case-control study, however, exposure misclassification could have been differential if cases had a better recall of exposure than controls. This probably occurred in the recall of unusual exposures that led to respiratory symptoms, such as inhalation accidents, and could have resulted in an overestimation of the associated risk. Nevertheless, differential recall between cases and controls is less likely to have occurred in questions referring to current exposures customarily performed.

A common limitation in studies of occupational health effects is the "healthy worker effect". This generic term includes two different types of selection bias: "selection into" and "selection out of" the workforce. The first problem, also known as "healthy hiring effect", is the result of the selection of healthier individuals to enter the workforce, leading to a better-than-average health status in those employed.[153] Taking into account that domestic cleaning work is an informal occupation, this selection is more likely to have occurred in an opposite way,[172] that is, that those entering the domestic cleaning workforce had a worse-than-average health status. If so, this could have resulted in an overestimation of the risks associated with domestic cleaning job in the population-based survey. The second component of the healthy worker effect has also been referred to as a "(healthy) survivor effect"[34] and takes place when those experiencing health problems quit their job, improving the health status of the workforce. In the population-based study, although minor, this survivor effect was present, resulting in an underestimation of the risks associated with current cleaning work.

In the case-control study, we assessed associations between respiratory symptoms and current frequency of exposure to each cleaning task and product. However, the current exposure pattern of an individual does not necessarily reflect exposures from the past, given that changes over time are expected to occur due to the introduction of new cleaning products, new technological advances or simply because of the acquired (occupational) experience of the individual. In addition, periods of unemployment and/or variations in the number of working hours during different periods of time are likely to occur in domestic cleaners, resulting in an additional source of exposure variability over time. All these changes in exposure, if unrelated to respiratory symptoms, could have resulted in a non-differential misclassification of exposure, biasing our results towards the null.[186] On the other hand, it is possible that subjects with respiratory symptoms have

experienced additional changes in their exposure pattern trying to avoid those exposures that bother them. This certainly occurred with the use of hydrochloric acid, abandoned by 20% of cases and 4% of controls due to respiratory health reasons. This selection bias resulted in the underestimation of the risk associated with hydrochloric acid, and possibly also with other irritant cleaning products.

Although we used validated questions from the ECRHS questionnaire[112] to define asthma and chronic bronchitis in our study, important changes in symptomatic status were observed between the population-based survey and the case-control study. Part of these changes was probably due to the inherent variability of asthma, which could have led to the remission of symptoms in some subjects and the onset of symptoms in others.[121] However, it is likely that part of these changes were also due to an important measurement error in self-reported symptoms. *A priori*, we did not expect this measurement error to be different between those working in domestic cleaning and those in the reference group. Thus, results in the population-based survey were probably biased towards the null.[186] In view of this error, in the case-control study we adopted a conservative approach by including as cases and controls only those persons with the same outcome in both phases. This probably improved the validity of our case definition, but precluded the analysis of incident cases and reduced the statistical power.

The limited knowledge about specific risk factors for respiratory morbidity in cleaning workers led us to examine a wide range of cleaning exposures. This could have resulted in some spurious associations, although the agreement between the case-control and the panel study and the consistency with surveillance programmes and case reports do not support this hypothesis. Finally, the small sample size in both the case-control and the panel study resulted in a limited statistical power for the analyses. In addition, in the panel study, the lack of within-individual variability for uncommon cleaning exposures forced us to

exclude them from analyses. These circumstances could have precluded the recognition of other potentially relevant associations.

8. CONCLUSIONS AND RECOMMENDATIONS

8.1. Conclusions

Domestic cleaning women have an increased risk of suffering asthma and chronic bronchitis symptoms as compared with women never employed in cleaning.

The risk of asthma and chronic bronchitis symptoms is more pronounced in former than in current domestic cleaning women, suggesting differences in exposure, the presence of a "survivor effect", or both.

Asthma and chronic bronchitis symptoms in domestic cleaning women are related to the frequent use of bleach and possibly also other irritant cleaning products.

Asthma and chronic bronchitis symptoms in domestic cleaning women are related to accidental exposures to high levels of respiratory irritants derived from cleaning agents. This predominantly occurs when inappropriately mixing bleach with other cleaning products or when using ammonia or hydrochloric acid.

Although distinction between asthma and chronic bronchitis symptoms was difficult in our study, the results suggest a more evident effect of irritant cleaning exposures on asthma than on chronic bronchitis symptoms.

Transient exposure to irritant cleaning products is related to the aggravation of lower respiratory symptoms in domestic cleaning women with a history of asthma and/or chronic bronchitis symptoms.

Taking into account the nature of the exposures associated with respiratory symptoms in domestic cleaning women, the mechanisms involved in the induction and/or aggravation of obstructive lung disease in this workforce are likely to be predominantly irritant-related.

8.2. Recommendations

One of the objectives of the EPIASLI study was to provide information for the establishment of preventive measures to protect the respiratory health of cleaning workers. Ideally, recommendations for the establishment of preventive measures should be based on sufficient understanding of the aetiology and dose-response relationships between cleaning exposures and respiratory disorders. The current knowledge about these issues does not allow for the establishment of a robust set of evidence-based preventive measures. Nevertheless, based on our findings in domestic cleaning women, and following the precautionary principle, some prevention strategies could be suggested for this workforce.

Traditional interventions in occupational health such as employees training or workplace safety regulations would result unfeasible here because of the informal nature of the domestic cleaning job. Therefore, preventive strategies aiming to reach the domestic cleaning workforce should probably be directed to the general population or specific target populations such as women with a low-educational level.

According to our results, prevention of cleaning-related respiratory symptoms should focus on the control of irritant cleaning exposures, either resulting from recurrent low-level exposure or from a single massive inhalation. Actions to prevent the first instance should include informative campaigns about the hazards of irritant cleaning products and the existence of non-irritant (or less irritant) cleaning products that can alternatively be used. However, cleaning workers may be reluctant to abandon the use of a highly effective irritant cleaning product if it allows them to perform their job with less effort and quicker than using a non-irritant cleaning product. For that reason, informative campaigns should also include tips for safe handling of irritant cleaning products and recommend measures to reduce exposure during use, such as ventilation of the room or leaving the room after application.

Strategies aiming to prevent accidental massive inhalations due to inappropriate cleaning mixtures should include community education about incompatible cleaning products. Data from poison control centres have shown that a considerable proportion of subjects involved in inhalation accidents due to cleaning mixtures is unaware of the hazards of such combinations.[91] Regulatory action to improve warning messages in consumer cleaning products to explicitly state any incompatibility with other cleaning products should be a priority. Nowadays, these warning messages are inexistent in many household cleaners sold in Spain, including dishwashing liquids.

Finally, although our results suggest that prevention strategies aiming to control irritant cleaning exposures should be prioritised, the limited knowledge about the specific occupational hazards in domestic cleaning workers justifies the promotion of broad-spectrum protective measures. These include measures such as ventilation of the working area or use of respiratory protective devices.

9. FUTURE RESEARCH

The main focus of the EPIASLI study was to investigate relationships between occupational exposures and asthma symptoms in cleaning workers, with a special emphasis in domestic cleaning workers. Here we have presented the results of the analyses focusing on current domestic cleaning women. Further analyses in the EPIASLI study include results from a case-control study of former domestic cleaners and a cross-sectional study of current non-domestic cleaners. These analyses will permit the identification of other cleaning exposures potentially related to asthma symptoms in cleaners and will help to account for the observed differences in asthma risks among the different cleaning groups. In addition, our research team is currently involved in the assessment of asthma risks related to specific cleaning exposures in the general population, as a part of the ECRHS-II.

Confirmation of our results by other studies within and outside Spain will help to reinforce the hypothesis that obstructive lung disease in domestic cleaners is mainly related to irritant exposures and to identify other specific exposures potentially related to asthma or chronic bronchitis symptoms in this workforce. Elucidation of whether asthma and chronic bronchitis symptoms are mainly new-onset or work-aggravated should be one of the focuses of further research in this field. As well, determination of the relative importance of RADS versus low-dose RADS in the occurrence of asthma in cleaners is relevant for directing intervention efforts. Further research is also needed to quantify the magnitude of cleaning-

related asthma and chronic bronchitis in other occupations and in the general population.

Finally, although the main focus of the EPIASLI study was to investigate respiratory health problems, during the study we also collected data on non-respiratory disorders, including skin symptoms, neuro-psychological disorders and musculoskeletal problems. This will allow further study of other health problems affecting domestic cleaning women.

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